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THE ANALYSIS OF MALARIA EPIDEMICS

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Introduction

Malaria, possibly the greatest epidemic disease, differs from most others in that its increases can often be attributed to a known cause which may be susceptible to numerical measurement, and in consequence the possibility of analysis is greater than in the case of other diseases. A series of papers has already been published (Macdonald, 1950a & b, 1952a & b) in which a theory of happenings in the transmission of malaria has been set out with reference to the parasite rate, the sporozoite rate, and the equilibrium of malaria, and in which previous literature on the analysis of events has been reviewed. In the present paper the theory of happenings is extended to

illustrate the nature and causation of epidemics. As in previous papers the argument is based on mathematical analysis which is presented separately in an Appendix (below, p. 883), while natural happenings and the implications of mathematical analysis are discussed in the text.

The word epidemic is used in its wide sense of an unusual prevalence, whether that occurs on a background of previous complete freedom from the disease or one of material incidence. This assimilation into one main group has been made despite the recommendation of the Drafting Committee of WHO (Covell *et al.* 1953), primarily because attempts at classification of natural happenings proved needlessly difficult if a distinction according to previous prevalence were insisted on. Epidemics or outbreaks are essentially similar whatever their circumstances, and distinction on differences in surroundings proves false when applied to actuality.

Analysis demands separate study of three aspects of epidemics; happenings during a single outbreak; the nature of and reason for epidemic series, and the precipitating causes of non-periodic outbreaks. These are treated separately in the text and the Appendix.

The Form of Single Outbreaks

The general form of seasonal curve of malaria in Europe was well understood by Hirsch (1883) and workers before him, but was first translated into parasitological terms by Celli (1900) who distinguished between types in northern and southern Italy. The distinction was elaborated by others, and most completely by Gill (1938) who produced a classified series of types for different climatic zones of the world. One must, however, agree with Pampana (1944) that even this classification was an over-simplification, there being as many types of epidemic curve as there are malarious countries, and innumerable sub-divisions without epidemiological point would be needed to describe them in full. The various curves are made of three components: relapsing or latent *Plasmodium vivax* malaria, fresh *P. vivax* infections and fresh *P. falciparum* infections. In the temperate zones of Europe relapsing and latent *P. vivax* malaria occurs as a wave starting early in the year and reaching a maximum in April or May, after which the cases decline in number. This curve is succeeded by a second one of fresh infections starting at the height of the summer, and the two usually merge into each other, producing a curve with two peaks separated by a trough of variable depth. *P. falciparum* infections, in those countries warm enough for transmission of this parasite, start as an abrupt wave at the height of summer about the same time as, or a little later than, the second wave of *P. vivax*. The relative sizes of these three components determine the characters of the total epidemic curve. In temperate countries the two *P. vivax* waves are marked, in warmer lands they become progressively less noticeable until the first of them disappears and the *P. falciparum* wave assumes a steadily greater importance. The increasing preponderance of the latter is commonly attributed to the higher temperature requirement of its extrinsic stage, which must play some part. It is noticeable, however, that the decrease of *P. vivax* is absolute as well as relative and it seems that the decrease of incidence in tropical countries is in very large part the result of the acquisition of immunity by the people. Moderate immunity results in suppression of the wave of relapses of *P. vivax* infections, and a higher degree in virtual suppression of summer outbreaks of new infections, at least in manifest form. The fact that the relative unimportance of the spring epidemic of relapses in subtropical countries is

a characteristic of the host rather than of the parasite is well shown by the experience of non-immune British troops in such countries, who have repeatedly experienced these spring epidemics when they were not suffered by the local people. It will be shown later that the multiplication of *P. falciparum* requires greater length of transmission season than does that of *P. vivax*, a feature which, together with its weaker stimulation of immunity, provides a better explanation of its geographical distribution than does the temperature requirement of the extrinsic stage.

The curve of *P. vivax* relapses has a smooth form and the production of gametocytes in its course provides an ample source for the development of the subsequent fresh infections. No such wave of *P. falciparum* relapses occurs and at the beginning of the transmission season its gametocytes may be rare; Bastianelli and Bignami (1900) drew attention to this and doubted the adequacy of the gametocyte reservoir as a source of the usual abrupt summer outbreak. Their opinions were based on findings in thin films, but the later development of the thick film technique revealed that gametocytes were less scarce than they had thought, although scanty. Ultimately Missiroli (1934) and other observers of the Italian School concluded that the reservoir was sufficient to account for the outbreak, a conclusion not accepted by all and notably not by Gill (1936, 1938). He had postulated an outbreak of relapses at the beginning of the 1934/35 outbreak in Ceylon, and proceeded to postulate that most outbreaks, including seasonal outbreaks of *P. falciparum*, began in this way. He did so because in his opinion the gametocyte reservoir must otherwise be quite inadequate, and the abrupt start of the *P. falciparum* wave and shape of the subsequent curve could not be explained in any other way. He drew largely on a sentence in a paper by Macdonald and Majid (1931) which referred to the geometrical increase of gametocytes, from which he deduced that if increase of this nature occurred there must be a series of cases at intervals of a month, separated by quiescent intervals, a conclusion which would have astonished the writers of the sentence. Gill's postulation of an epidemic of relapses met with immediate criticism on the grounds that no evidence of such relapses of *P. falciparum* had been produced. The small gametocyte reservoir had previously been shown to be adequate, but the difficulties presented by the abrupt rise and subsequent shape of the wave were not explained, and there is in consequence a lingering desire to find some other explanation for them than the simple mechanistic one of progressive multiplication of fresh infections.

In the Appendix to this paper is presented a mathematical analysis of an outbreak based on entirely mechanistic assumptions, there being a previous reservoir of parasites, possibly very small, and the actual amount of previous transmission being small or negligible. It is postulated as a basis for argument that on a given day one or more of the factors essential for transmission is changed in such a way as to make transmission more frequent, but whether by increase of mosquito numbers or longevity, or by change of temperature, or mosquito biting-habit, is immaterial. The subsequent multiplication of cases is followed in mathematical form both as the proportion affected, which is related to the parasite rate, and as cases positive for the first time, which is related to the reported morbidity. The general form of the resultant curves is shown in Figure 1 and is particularly characterized by an abrupt initial rise in the new cases, followed by

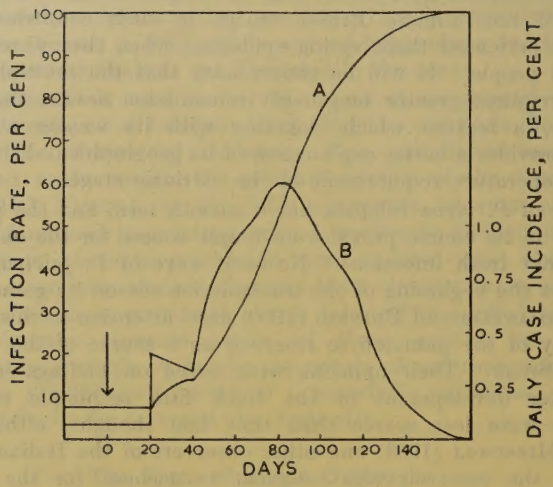

FIGURE 1

Diagrammatic curves illustrating (A) the change in the infection rate and (B) the incidence of fresh infections, according to a mechanistic theory of insect-borne diseases presented in the Appendix. The arrow indicates the time when conditions favouring the epidemic start, the combined incubation period in insect and man being 20 days. Both curves fall into two distinct parts, the division being more readily noticeable in the curve of fresh infections. The relative scale of the two parts and the time scale depend on the value of several variables.

a pause, during which in the pure form there is some actual decrease in new cases, in turn succeeded by a second wave ascending in a slightly irregular way to a peak. The abrupt change from unfavourable to favourable transmission conditions is probably not the rule in nature, where blurring of this outline would be expected. The blurring is not always great and the curves of the Ceylon epidemic (BRIERCLIFFE 1935), one of which is shown in Figure 2 and which have caused difficulty in interpretation, nearly follow the mathematical form, showing that it is unnecessary to postulate any cause other than an abrupt change in transmission factors to explain them. This change was probably the sudden emergence of anophelines from pools formed by the rains which broke the drought shortly before the epidemic started.

The curves shown in Figure 1 are diagrammatic in that they represent general mathematical formulae incorporating several variables, the relative value of which could greatly influence the time-scale of the epidemic and the proportions of the two parts of the curves. It is of interest to explore the order of values which could produce a happening such as that of 1934/35 in Ceylon, and Figure 2 shows a synthetic curve prepared to correspond with that observed. It is not presented as an exact rebuilding of the natural happening, for which the data are inadequate, but as a presentation of circumstances which could produce an equivalent result, and are thought to resemble those actually present. The values selected are given in the Appendix; the change which precipitates the synthetic outbreak is a multiplication in anopheline density by 5·3 at a time when conditions are

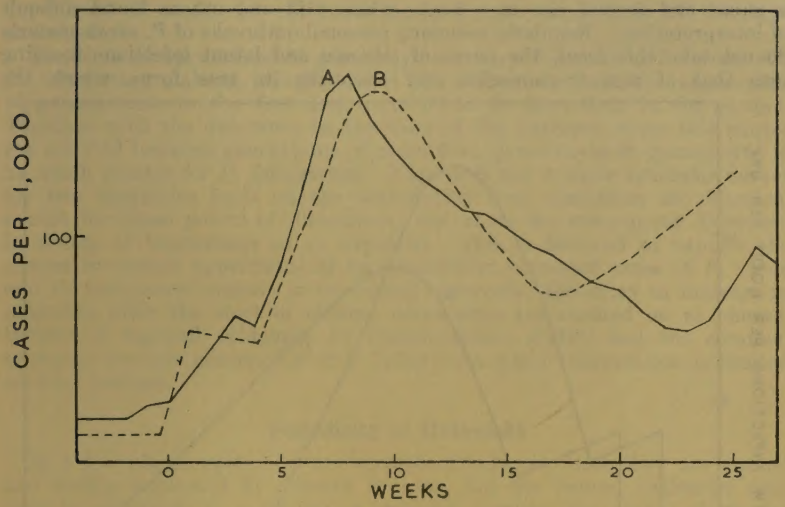

FIGURE 2

The actual epidemic curve of the Deduru Oya Basin, Ceylon, in 1934–35 (A), and a synthetic curve (B) built to resemble it on data presented in the Appendix. In this latter each fresh infection has been credited with 1·8 attendances in order to bring the total of attendances in the two occurrences to the same figure. The final increase in the synthetic curve is due to late appearance of *P. falciparum* infections.

favourable to moderate longevity and on a background of slight transmission only. The basic reproduction rate (MACDONALD 1952b) of *P. vivax* malaria during the synthetic outbreak is 7·3, having been increased to this value from 1·375 by an equivalent increase in anopheline density. A similar change, with nearly the same results, would have been produced by a change in the anthropophilic index from 10 per cent. to 23 per cent. or by a change in the probability of mosquito survival through one day from 0·8 to 0·9, though in this case it would be necessary to postulate a different anopheline density from that here used. It appears that such is the order of events needed to precipitate an outbreak of the scale seen in Ceylon where the vector involved is one associated with the epidemiological type previously described as unstable (MACDONALD 1952b).

RAJENDRAM and JAYEWICKREME (1951) have since published details of several other outbreaks in Ceylon, and RAJENDRAM (1952) has provided weekly morbidity figures for 4 years in 10 areas liable to epidemics. They cover 34 outbreaks, in 19 of which the initial abrupt rise is followed by a pause before the second rise to the peak, an occurrence which is therefore common in other years than 1934. Comparison with the associated rainfall records makes it justifiable to assert that this form was usual in epidemics following light rains breaking a drought, whereas those following unusually heavy rains showed no such break. The present writer's interpretation is that the first type is due to an increase in anopheline numbers which tends to be abrupt, while the second is due to change in mosquito longevity which is more gradual, though for certainty this second interpretation requires more supporting data than are available.

Seasonal outbreaks of *P. falciparum* malaria commonly take the form here described, and in fact it is the characteristic of abruptness, frequently with

a pause and second rise to a peak, which Gill and others found difficult of interpretation. Regularly recurring seasonal outbreaks of *P. vivax* malaria do not take this form, the curve of relapses and latent infections merging into that of new transmission and obscuring its true form, which the

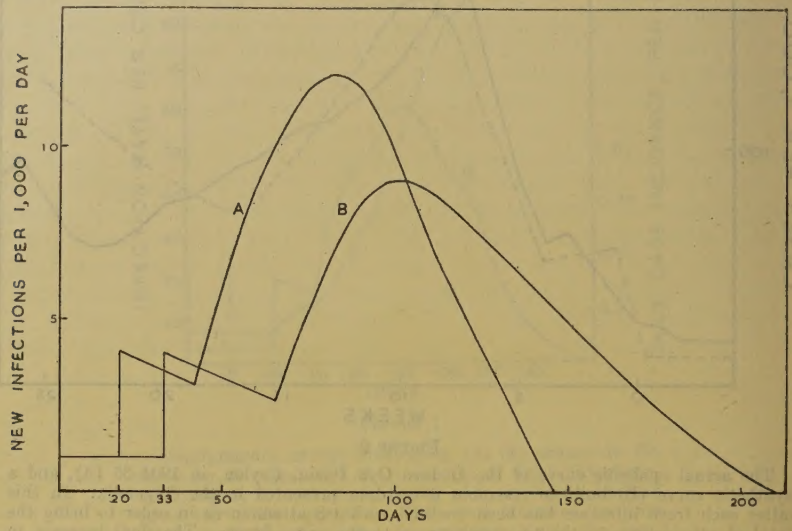

FIGURE 3

Synthetic curves of fresh infections in two epidemics of malaria built on identical data except that in A the extrinsic cycle lasts 9 days and the total incubation period, gametocyte to gametocyte, is 20 days, whereas in B the periods are 12 and 33 days respectively. The curves are intended to represent the *relative* timing of *P. vivax* and *P. falciparum* outbreaks, though the actual timing and the scale of the two parts of the curves might be greatly different.

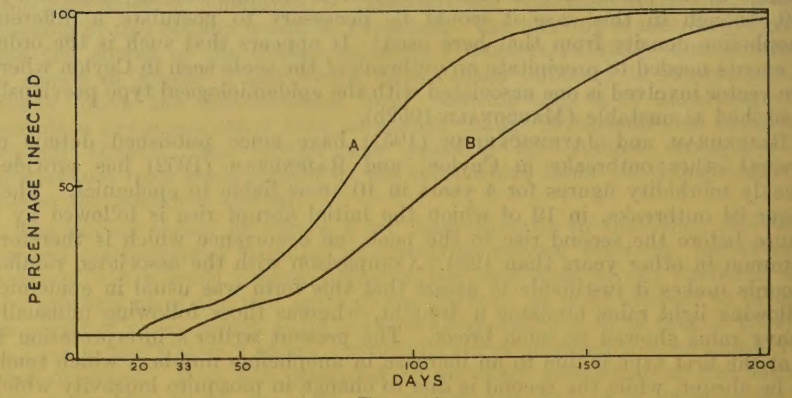

FIGURE 4

Synthetic curves of the infection rate in two epidemics similar to those of which fresh infections are shown in Figure 3. The effect of abbreviation of the transmission season in discouraging the multiplication of *P. falciparum* can be inferred from the relative rates of ascent of the two curves.

experience of occasional non-recurring outbreaks suggests is of the type described.

The time of appearance of gametocytes is very different in *P. vivax* and *P. falciparum* malaria, usually about simultaneously with the appearance of parasitaemia in the first and some 10 to 15 days later in the second. Together with the difference in the time of the extrinsic cycle this causes the interval between generations of cases from gametocyte to gametocyte to be much greater for *P. falciparum*. Figures 3 and 4 show synthetic curves for two epidemics built on the assumption that conditions are identical except for these points of distinction, and show the consequent difference in timing of happenings to be expected. This is believed to explain the almost invariable appearance of two successive waves of cases of *P. vivax* and *P. falciparum* malaria in occasional outbreaks, the delay in increase in mortality after the start of clinical happenings commented on as characteristic of regional epidemics by Christophers (1949), and the common tendency towards elimination of *P. falciparum* when transmission is limited to brief periods.

Periodicity of Outbreaks

In a few places epidemics are occasional only; in most they are annual and readily explained by climatic seasons, but the annual epidemics may vary in amplitude in a regular or irregular manner, the period of regular cycles varying from 5 to 20 years in length; these periodic cycles are sometimes in turn only features of greater waves with a length of a century or more.

Short-term cycles

The occurrence of the shorter cycles has long been recognized; Hirsch (1883) described a series of outbreaks at intervals of 20 years in Europe between 1718 and 1860, which provide a background for the roughly 20-year cycle from 1880 to 1946 described by Swellengrebel (1950) in Holland. Celli (1910) described a cycle in Italy. Christophers (1911) showed one in northern India and Pakistan which has later been analysed by Gill (1928) and Swaroop (1949) and almost certainly has an 8-year period. A similar period of 6 years has been demonstrated in Ceylon by Briercliffe (1935) and Rajendram and Jayewickreme (1951). Gabaldón (1949) has shown the occurrence of a roughly 5-year periodicity in Venezuela, British Guiana, Dutch Guiana and Cuba. The occurrence of 20-year periodicity in part of Argentina and the State of São Paulo in Brazil has been documented by Barbieri (1931), and Faust (1945) produced evidence of a 5-year period in the United States. In a few places the variation in amplitude is extreme, as in the Punjab, Ceylon and Argentina, and in such places happenings have been distinguished by the title of "regional epidemics". Distinction on grounds of amplitude seems quite artificial though it may be convenient, and a continuous series can be observed, with at one extreme the fulminant outbreaks of Ceylon and India, and at the other the mild ones of Holland or the Caribbean.

Long-term changes

Waves with much longer periods have been described for one small area, the Agro Romano, over 1,500 years by Celli (1925), who demonstrated four periods of exacerbation in this time. Hirsch (1883) described the gradual decline of malaria in northern Europe which started some time in the eighteenth century and which has progressed past his time to the present. The trend is undoubtable though it has been broken by periodic increases

and by occasional irregular exacerbations as in the Napoleonic wars, the 1914–1918 war, the Spanish Civil War and the 1939–45 war. It is matched by a wave in the U.S.A. of which both the increasing and decreasing aspects have been documented by Boyd (1941) and Faust (1945); it started in the seventeenth century, reached its peak about 1870 and was declining to probable natural extinction when accelerated by recent control programmes. This decline may cover a much larger territory than the U.S.A., and has been described in Jamaica by Boyd and Aris (1929). There are many detailed analyses of local happenings, such as that for England by James (1929), and studies of their possible cause. Changing husbandry and housing, and lessened contact between man and the mosquito due largely to deviation of anophelines to animals following the increasing practice of stabling animals, have been generally accepted as an explanation. One of the most analytical studies, by Brumpt (1944), rejects both the term " spontaneous " regression and this cause, as the decline is not confined to places where farming practices have altered. This author considered that the main cause has been a reduction in the gametocyte reservoir partly due to increasing medication and partly due to changing birth rates resulting in changing proportions of children in the population. These immediate causes were favoured by increasing prosperity and education, and by migration from the countryside of the more poverty-stricken inhabitants.

The cause of short-term cycles

The mathematical aspects of variability are explored in two sections of the Appendix, where there is developed a simplified index of stability derived from those previously published, and an exploration of the influence of the recovery rate on malaria incidence. This exploration emphasizes the influence of anopheline longevity and biting-habit on the stability of the disease, and does so in a simple form which leaves the average number of bites on man taken by an anopheline during its lifetime, a combination of biting-habit and longevity, as the main controlling factor. Indeed this average number of bites is so influential in this respect that it can properly and readily be used as an index denoting the probable characteristics of the disease conveyed by any particular variety of mosquito.

When the average number of feeds is small, there results a great instability of equilibrium manifested by a tendency to fluctuations, the scale of which exaggerates the stimuli which cause them; thus in such a case a 10 per cent. increase in anophelines can cause a 100-fold increase in malaria, whereas such exaggeration would not occur if the vector fed frequently on man, though of course the basic numbers of mosquitoes needed to keep transmission going at all would be quite different in the two cases. This exaggeration may lead to rapidly explosive outbreaks once the basic threshold is passed, which in turn are the stimulus to development of immunity comparable in degree to that of the outbreak causing them. Immunity does not, however, appear at the same time as the stimulus; in the case of *P. vivax* it appears in sufficient degree to limit transmission a month or two later, a fact well illustrated in a field experiment at Torpé, Sardinia, by Missiroli (1933). In the case of *P. falciparum* its appearance may be much longer delayed.

The effect of resistance is to limit transmission by reduction of the gametocyte reservoir. The interval between its stimulation and appearance, and thus reduction of stimulus, may permit transmission to pass the point of balance which would be achieved if the two occurred simultaneously. Rapidly developing outbreaks may therefore stimulate the production of

more immunity than is needed merely to restrain them, and which is indeed sufficient to bring them to an end, a point developed by Missiroli (*loc. cit.*).

Exactly those circumstances which exaggerate the response to increased transmission, a low average number of feeds on man by the mosquito, also exaggerate the effect of increased immunity in restraining transmission, as is demonstrated in the Appendix. Outbreaks in these circumstances may therefore be expected to lead to one of two results. If the closure of the epidemic is sufficiently abrupt it may bring transmission to a total end and result in local extinction of the disease; if it is less abrupt it may lead to partial suppression of transmission, followed by loss of immunity and re-emergence of the disease to re-start the cycle of alternating epidemic and quiescent periods. The first of these is the probable happening in those many epidemics in usually non-malarious lands following importation of gametocyte carriers, which have grown to a peak and then waned to total disappearance, and the natural elimination of *P. vivax* from some Caribbean islands and even from parts of tropical Africa where malaria is seasonal may well be explained in this way. The second is the precursor of periodic fluctuation on a regular cycle, such as has been shown to exist in many parts of the world and which mathematical examination suggests is likely wherever the disease is carried by mosquitoes which do not normally feed frequently on man. The mechanism of this periodicity has been amply demonstrated in Holland by Swellengrebel (1950), and others. Following the outbreak transmission comes to a virtual end among the general population and is kept up only in those localities where there are many infants, that is in places where the communal resistance is most rapidly diluted. After a time, following dilution of the resistance in the general populace, the disease overflows from its restricted foci to the people at large, mounts into an epidemic and again subsides. It seems very probable that this inter-epidemic restriction to limited foci occurs in northern India and possibly elsewhere, and its verification should lead to improvement in the methods of epidemic control.

Fluctuation may be of any degree and, if it is to be characterized by dramatic fulminant outbreaks, certain requirements must be met. Transmission in the intervals must be reduced to negligible amount; the gametocyte reservoir must be adequate when an outbreak becomes due, and transmission must be maintained for sufficient time for full development of an outbreak, about the time of three generations of the parasite from gametocyte to gametocyte, some 60 days for *P. vivax* and 90 days for *P. falciparum*. These requirements are only commonly met in limited areas which are the notorious epidemic areas of the world, such as northern India and parts of Ceylon.

The analysis in the Appendix shows, on the other hand, that when the vector feeds frequently on man an increase in anopheline density, or the like, produces a much slighter effect on transmission and thus a lesser change in immunity. Moreover, it can be seen from expression (21) that growing immunity is less likely to lead to extinction of the disease or even its reduction to negligible amount. Since changes in transmission and in development of immunity are likely to be less abrupt, and because the effect of immunity in restricting transmission is less, there is a much greater likelihood of stable equilibrium being established. A dampening effect on the influence of increasing resistance in this case is implicit in the expression quoted, and it would need a remarkable over-stimulation of resistance to prevent the establishment of balance between it and transmission.

Fluctuation and either natural disappearance of the disease or periodic exacerbation on a regular cycle therefore appear to be a natural result of

those mosquito characteristics of longevity and biting habit which make it unlikely that the average vector will take many feeds on man, and which thus reduce the probability of one mosquito infection being masked by a previous one. Freedom from fluctuation and from periodic cycles is to be expected when malaria is carried by mosquitoes which on the average feed frequently on man, a feature which favours the masking mechanism and its operation like the governor of a machine, always tending to produce equilibrium.

The cause of long-term changes. Long-term variations have been variously explained by changing density of vector anophelines, their deviation to animals by changing husbandry, medication, decreasing child population and other causes. An examination of the very small margin which may separate severe transmission and elimination shows how easily, with only minor discernible change, any one of these factors could produce the result of dramatic increase or decrease in malaria, and the production of waves by changing civilization is therefore fully explicable in all those places infested by zoophilic anophelines associated with unstable endemicity. The necessary changes are so slight that analysis of the detailed causes of historic happenings would be very difficult. The indication from them that waves occur, and that an elimination which appears spontaneous is possible even from some highly malarious places, should be a stimulus to research in other countries. Enquiry is particularly justified in places where malaria is maintained by zoophilic anophelines, as there is sufficient *prima facie* ground for believing that comparable elimination could be encouraged in many of them.

Non-Periodic Outbreaks

The literature abounds with accounts of individual outbreaks, a full review of which would serve no useful purpose. Precise accounts containing full data are rare, however, and incomparably the most nearly complete is that by Covell and Baily (1932) of one in Sind, which is particularly remarkable for the serial records of oöcyst and sporozoite rates corresponding to the parasite rates. Taken together with other data they indicate an unusual proliferation of anophelines before the outbreak at a time when they were short-lived, and a later considerable increase in longevity which caused a second wave. Selection of other accounts is invidious but the author has profited particularly from accounts by Schüffner (1938) of one in Indonesia, by Ambialet (1940) and Parrot, Catanei and Ambialet (1940) in Algeria, and from a small but unusually prolonged study of happenings in a Saharan oasis by Hugonot (1950). The general form of happenings corresponds to that described in a previous section and is differentiated only by degree from that described by Christophers (1949) in his account of regional epidemics. The relatively late occurrence of *P. falciparum* infections, their particular association with prolonged transmission seasons and tendency to disappear in the early stages of control and re-appear later on its breakdown is notable in many records. The time of re-appearance and relatively slow multiplication is well shown in the accounts of Saharan and Spanish outbreaks by Hugonot (*loc. cit.*) and Rico-Avello y Rico (1950) already mentioned.

The localities involved, and the causes to which these non-periodic outbreaks are attributed, are innumerable but fall into a general pattern. Accounts of major outbreaks in the zone of distribution of the highly anthrophilic mosquitoes are relatively rare, and such as there are mostly refer to happenings in marginally malarious places especially where transmission is limited by dryness, or to the effects of gross changes in environment. Thus

epidemics are not infrequent on the margins of the area in which *A. gambiae* is the main vector, in Somaliland (Wilson 1949; Moise 1951), South Africa (Schoeman 1951) and on the heights of Kenya (Garnham 1945, 1948) where *A. funestus* may also be responsible (Heisch & Harper 1949). There are many records of epidemics in North Africa where dryness normally impedes transmission by *A. m. labranchiae* (Colligxon 1940, 1947; Ambialet 1940; Guerrieri 1950; Clastrier 1942, and others), but in the centre of this mosquito's zone in Italy such epidemics as are reported mainly follow gross disturbance of breeding or major movements of people, as in war. Some of these are summarized by Canaperia (1946).

The accounts of epidemics in the area of distribution of the zoophilic mosquitoes are, on the other hand, very numerous, they refer to epidemics in practically all parts of the areas infested, and the causes which they attribute are often very slight and sometimes difficult to trace. This distinction of the probability of and the severity of the causes precipitating the epidemics within the zones of the two types of vectors is very noticeable. Basically the causes are the same wherever epidemics happen and may be classified in the following way:—

1. *Introduction of the malaria parasite.* The most dramatic example of this is the introduction of malaria into the Americas some time in the sixteenth century, the history of which has been reviewed by Boyd (1941). Most other records are of probable re-introduction to places whence the disease had previously disappeared. A recent case of re-introduction occurred in Grand Canary (Garcia Sastre 1945); the original case was probably identified and the course of events documented in some detail. Similar re-introduction has recently occurred in many parts of Europe, and as an example occurrences in Czechoslovakia are described by Snuparek (1947). It seems very probable that such re-introduction usually leads to natural disappearance again after an epidemic, as the result of a mechanism already described.

2. *Introduction of anophelines.* Most records concern the migrations of *A. gambiae*—to Mauritius in 1865 (Ross 1908), to Durban (Murison 1910), to Brazil (Soper and Wilson 1943) and Egypt (Shousha 1948). The high vectorial capacity of this species would make migration more obvious than that of most species, but general faunal distribution suggests that few anopheline species have made comparable journeys. The migration to Brazil is the sole one fully documented and is remarkable for the long period of 7 years taken for full establishment and multiplication sufficiently to cause major outbreaks.

3. *Numerical increase in anophelines following human activity.* Man-made malaria is notorious and universal. The great examples come from areas infested by highly zoophilic species; many from that of *A. culicifacies* in India. They include the epidemic increase in northern India following canal construction, the account of which by Baker, Dempster and Yule (1847) was remarkable for delimitation by the spleen rate and exact attribution of causes. Later examples include the Cauvery Canal Project, the effects of which are described by Russell (1938), and the Sind irrigation responsible for the outbreak described by Covell and Baily (*loc. cit.*). Such major regional disturbances appear to be mainly conversion of a pre-existing anophelism without malaria into an epidemic condition by increase of anopheline numbers, which may be relatively slight. Natural elimination can occur from such areas if the critical density is not greatly exceeded, and this has been seen in parts of the area affected by the Cauvery outbreak.

4. *Migration of non-immune people.* The malaria associated with aggregation of labour in the tropics is well recognized. The frequent occurrence of aetiologically similar outbreaks unassociated with labour forces is less accepted. War and post-war outbreaks must largely be attributed to this cause. Rico (1950) found migration of non-immunes the most prominent background of the Spanish outbreak of 1939–43. It is clearly commented on in the Italian epidemics described by Raffaele and Coluzzi (1949), Sani (1950), Garaci (1947) and others. These epidemics reached their peak some years after the battles had passed, and though physical disturbance causing proliferation of anophelines contributed to some, it could not be brought to explain all, and specially not the Spanish happenings. These occurrences were in places where resistance probably greatly restrained transmission, and the dilution of resistance by migration of non-immunes could cause great increase in transmission, or even explain the actual difference between anophelism without malaria and epidemics. The Macedonian outbreak of the twenties, and the Russian one of 1921, are probably examples of the same aetiology.

5. *Deviation of anophelines from animals to man.* Deviation to man may be due to deprivation of cattle, often following war, as described in Okinawa by Downs (1949) and in Italy by Canaperia (1946), or by invasion of towns containing few cattle by normally zoophilic anophelines. Covell and Jaswant Singh (1943) gave a detailed account of such a case in Delhi, and a similar event has also been described in Indo-China by Toumanoff (1952). Such deviation is a probable major contribution to malaria associated with labour forces, who in the early stages of their development do not usually own cattle.

6. *Climatic changes.* The effects of climatic variation are most marked on the margins of the distribution of malaria whether in tropical or cooler zones. The varying influence of rainfall in producing or destroying breeding places is well understood. Attention was drawn to the effect of increasing humidity on mosquito longevity and thus on transmission in India by Gill (1928), and it appears to be a prominent cause in many outbreaks. It was well substantiated as the reason for a dramatic outbreak in Maracaibo, Venezuela, by Nieto Caicedo (1946), and has been reasonably put forward as an explanation of the great epidemics in Argentina which follow flooding but are not confined to flooded areas (Alvarado 1942). Prolongation of the warm season permitting increased transmission may also be an important influence in northern Europe and elsewhere as in Morocco (Messerlin 1941) and the inland territories of South America (de Mello 1948).

Though the immediate cause of such outbreaks is varied, the basic cause is commonly single; instability due to transmission by anophelines which under local conditions do not often bite man, or to transmission at temperatures unfavourable to extrinsic development, conditions in which minor modification of transmission can greatly modify incidence. The tendency to epidemics is only part of a picture, the other part of which is tendency to reduction which may end in natural elimination or which can be artificially encouraged to this end. The experience of natural decline strongly suggests that pride in the new development of insecticides should not lead to their exclusive use but should permit a continued study of other methods, such as modifications in animal maintenance, which may reinforce and eventually act as substitutes for insecticides in some parts of the world in precipitating an apparently spontaneous regression.

Summary

The form of epidemic curve is briefly discussed and the difficulties encountered in its explanation are referred to. A mathematical analysis of expected happenings following sudden increase in transmission is presented, together with curves illustrating it. They show the characteristics found difficult to explain in natural happenings, including abrupt onset and later pause in the ascent to the peak, and may be taken as adequate representations of them.

A synthetic epidemic resembling that of Ceylon in 1934 is presented and it is shown that comparable happenings could be produced by an approximately five-fold increase in the anopheline density at a time when the prospects of anopheline survival were good, or by a change in the anthropophilic index from 10 to 23 per cent., or by an alteration in the probability of mosquito survival through one day from 0·8 to 0·9.

The frequent occurrence of epidemic curves in Ceylon resembling this synthetic curve is noted.

The effect of prolonged extrinsic cycle and delayed appearance of gametocytes is to delay the multiplication of *P. falciparum* relatively to *P. vivax*, thereby producing the relative timing of outbreaks which is common and accounting for the dependence of the former species on relative length of transmission season.

Variations in incidence other than annual variations are analysed as periodic, long-term, and irregular. Periodic curves occur on cycles varying from 5 to 20 years in length, the amplitude of the wave ranging from the extremes of regional epidemics in the Punjab and Ceylon to small outbreaks in Holland. The influence of stability of malaria as determined by the longevity and biting habit of the vector on these variations is analysed mathematically and discussed in the text. It is shown that the effect of instability must be a tendency to either local extinction of the disease following an epidemic, or to periodic fluctuation which is therefore regarded as a characteristic of instability. The reason why malaria transmitted by anthropophilic mosquitoes tends to become stabilized is also demonstrated.

The form of long-term variations in Europe and North America is discussed. Analysis shows that very small changes in the essential transmission factors could cause them though identification of the reason might be very difficult. The greatest significance of these long-term changes is the demonstration of the possibility of local extinction of the disease following minor changes in husbandry, which could happen in some other areas.

Non-periodic outbreaks occur within the distribution of highly anthropophilic vectors but are usually due to obvious gross causes, or occur on the margin of their distribution. The literature abounds with reports of such outbreaks elsewhere and a classification of their causation is presented.

Appendix

MATHEMATICAL STATEMENT

Symbols

Symbols are used with the following meanings:—

- m the anopheline density in relation to man.
- a the average number of men bitten by one mosquito in one day.
- b the proportion of those anophelines with sporozoites in their glands which are actually infective.

p the probability of a mosquito surviving through one whole day.
n the time taken for completion of the extrinsic cycle.
s the proportion of mosquitoes with sporozoites in their salivary glands.
h the proportion of the population receiving infective inocula in one day.
x the proportion of people affected (that is, showing parasitaemia).
L the limiting value of the proportion of men infected when equilibrium is reached.
r the proportion of affected people, who have received one infective inoculum only, who revert to the unaffected state in one day.
t time in days from the start of the incubation interval referred to.
e the base of natural logarithms, 2·71828.
i the average time in days from ingestion of gametocytes by an anopheline to the development of infective gametocytes in a secondary case infected by it. Successive intervals of this duration are designated i_0, i_1, i_2, etc. In wording, the period is referred to as the incubation interval.
y the proportion of total time lived, within one incubation interval, in which the population are infective, or

$$\frac{1}{i}\int_{t=0}^{t=i} x.\,dt$$

Expressions already established

All those listed in the Appendix to a previous paper (Macdonald, 1952b).

The form of outbreaks

Let it be assumed that malaria is endemic, a state of equilibrium having been reached, the value of x being low. This pre-existing equilibrium is expressed by:

$$\mathrm{L} = x_o = \frac{mabp^n}{r} + \frac{\log_e p}{a} \quad \text{(already established)} \quad .. \quad .. \quad (1)$$

and is due to an inoculation rate $mabs$, or:

$$h = \frac{ma^2bp^n x_o}{ax_o - \log_e p} \quad \text{(from value of } s\text{, already established)} \quad .. \quad .. \quad (2)$$

$$= x_o r \quad \text{(from the value } \mathrm{L} = \frac{h}{r}\text{, already established)} \; .. \quad (3)$$

from which it may be noted that:

$$ma^2bp^n = r\,(ax_o - \log_e p) \quad .. \quad .. \quad .. \quad .. \quad (4)$$

At a given time, starting the first incubation interval of a consecutive series, it is assumed that the value m, a or p is changed and that as a result the value of h is increased to ch, or $cx_o r$, during that interval. During the whole of it, however, there is no disturbance in the value of x, as by definition of i no secondary cases due to the increased value of h have yet occurred. Therefore $x_1 = x_o$. In the following interval, i_2 the value of x will show progressive increase. This increase will be in response to a static inoculation rate at its new higher value, ch. It is thus an independent happening and will follow the expression established for such, which taken with (3) reads:

$$x_2 = cx_0 - (cx_0 - x_0)\, e^{-ri} \quad .. \quad .. \quad .. \quad .. \quad .. \quad (5)$$

$$= x_0\{c - (c-1)\, e^{-ri}\} \quad .. \quad .. \quad .. \quad .. \quad .. \quad (6)$$

and $$\int_{t=0}^{t=i} x_2 .\, dt = x_0 ci - \frac{x_0}{r}\,(c-1)\,(1-e^{-ri}) \quad .. \quad .. \quad .. \quad .. \quad (7)$$

Since the total time lived in this interval is i days, and the number of infective days lived is given by (7), it follows that the proportion of time lived in which the subjects are infective is:

$$y = x_0 c - \frac{x_0}{ir}\,(c-1)\,(1-e^{-ri}) \quad .. \quad .. \quad .. \quad .. \quad .. \quad (8)$$

In the succeeding intervals, i_3, i_4, etc., the value of x again progressively increases, but now in response to a progressively increasing inoculation rate dependent on the value of x at the same stage in the previous incubation interval. The exact mechanism of this dependence from day to day for the period i_3 is demonstrated elsewhere by Armitage (1953, below, p. 890). For later periods i_4, i_5, etc., the expression and working become too complicated to be justifiable. The growth can, however, be approximately studied as serial values of x at intervals of time i starting from any desired point by the following method.

The value of y_2 is given in (8). The mean inoculation rate derived from it is expressed by:

$$h_2 = \frac{ma^2 b p^n y_2}{ay_2 - \log_e p} \quad .. \quad .. \quad .. \quad .. \quad .. \quad .. \quad (9)$$

$$= \frac{r\,(ax_0 - \log_e p)\, y_2}{ay_2 - \log_e p} \text{ (see (4))} \quad .. \quad .. \quad .. \quad .. \quad (10)$$

This new inoculation rate may be used in the expression for the value of x at the end of the interval i_3 when $t=i$:

$$x_3 = \frac{h_2}{r} - \left(\frac{h_2}{r} - 1\right) e^{-ri} \quad .. \quad .. \quad .. \quad .. \quad .. \quad (11)$$

The value of y_3 derived from this is:

$$y_3 = \frac{h_2}{r} - \frac{1}{ir}\left(\frac{h_2}{2} - 1\right)\left(1 - e^{-ri}\right) \quad .. \quad .. \quad .. \quad .. \quad (12)$$

and in turn

$$h_3 = \frac{r\,(ax_0 - \log_e p)\, y_3}{ay_3 - \log_e p} \text{ (see (2) and (4))} \quad .. \quad .. \quad .. \quad (13)$$

Approximate values of x at serial intervals can then be obtained by continuation of this process, and the derivative can be calculated at any point by the established expression:

$$\frac{dx}{dt} = h - rx \quad .. \quad .. \quad .. \quad .. \quad .. \quad .. \quad (14)$$

At the point in this series when the value of h exceeds r a transfer must be made to the basic formula:

$$x = 1 - (1 - x_0)\, e^{-ht} \quad \text{(already established)} .. \quad .. \quad (15)$$

which demands a modification of technique, but no more.

In the examples used in the text, among others, it was desirable to calculate a value of x for each successive day of several incubation intervals. This was performed by calculating serial daily values of x_2 by the basic

formula and thence deriving value of the sporozoite rate, inoculation rate and resultant derivative of x for each day starting at the beginning of interval i_3. The work is boring but properly set up is a simple repetitive matter, not unduly laborious. The general picture is, however, more readily derived by the method above described which, with proper setting, is very simple to perform.

In preparing the curves resembling those of the 1934–35 outbreak in Ceylon the following values have been used:—

m,	before origin of epidemic:	1·875
m,	after origin of epidemic:	10
a		0·05
p		0·9
n,	*P. vivax*	9 days
n,	*P. falciparum*	12 ,,
i,	*P. vivax*	20 ,,
i,	*P. falciparum*	33 ,,
x_0,	*P. vivax*	0·075
x_0,	*P. falciparum*	0·01

Peak is reached at 40 days after start (actual about 30 days)

Proportion of total cases in peak week 0·045 (actual 0·06)

Maximum sporozoite rate 10 per cent. (actual 8·6 per cent.)

The measurement of stability of malaria

The endemic level has previously been studied and established as:

$$L_x = \frac{mabp^n}{r} + \frac{\log_e p}{a} \quad .. \quad .. \quad .. \quad .. \quad (16)$$

and the basic reproduction rate as:

$$\frac{ma^2bp^n}{-r\log_e p} \quad .. \quad .. \quad .. \quad .. \quad (17)$$

No symbol has as yet been given for the last rate, but if it is here known for convenience as z, then it can readily be shown that:

$$L_x = \frac{-\log_e p}{a}(z-1) \quad .. \quad .. \quad .. \quad .. \quad (18)$$

and if the values 1 and 0 are successively attributed to L_x the successive values of z are:

$$\text{for } L_x = 1 : z = 1 - \frac{a}{\log_e p} \quad .. \quad .. \quad .. \quad (19)$$

$$\text{for } L_x = 0 : z = 1 \quad .. \quad .. \quad .. \quad (20)$$

whence the statement that the minimum increase in the basic reproduction rate necessary to raise x from 0 to 1·0 is: $\frac{a}{-\log_e p}$. This in fact also directly expresses the probability of the anopheline vector feeding on man during its life time. It is a convenient measure of stability of insect-borne disease.

The influence of the recovery rate on the endemic level

The partial derivatives of the limit of x with reference to each of the essential controlling or independent factors m, a, p, n and r have already been presented (Macdonald, 1952b).

The total derivative can readily be produced from these expressions; for the sake of simplicity, however, the derivative with respect to m and r only as independent factors is given below, the others being treated as constants:

$$d\mathrm{L} = \left(\mathrm{L} - \frac{\log_e p}{a}\right)\left(\frac{dm}{m} - \frac{dr}{r}\right) \quad .. \quad .. \quad .. \quad (21)$$

This shows that an increase in mosquito density can be balanced by a proportionately equal increase in the recovery rate. The effect of lack of balance in the increase of the two is, however, very greatly exaggerated when either or both p and a are small. On the other hand, when they are considerable there is little exaggeration, and indeed an actual diminution of effect when L is low.

The degree of this exaggeration and diminution may be illustrated by numerical values believed to represent happenings in nature. If $p=0{\cdot}75$ and $a=0{\cdot}025$ disparity in the values of $\frac{dm}{m}$ and $\frac{dr}{r}$ is exaggerated 11·5 times when $\mathrm{L}=0$ and 12·5 times when $\mathrm{L}=1{\cdot}0$. If $p=0{\cdot}95$ and $a=0{\cdot}5$, disparity is exaggerated 0·1 times when $\mathrm{L}=0$ and 1·1 times when $\mathrm{L}=1$. These examples do not appear to be extreme cases.

The effect of gross exaggeration of disparity when an increase in m is not simultaneously accompanied by an increase in r must be to produce an exaggerated increase in L. If, however, it is followed by an increase in r proportionately greater than that of m it must be followed by an exaggerated decrease in L which could well be reduced to zero by an only slightly excessive increase in r. Such a system is necessarily highly unstable and likely to result in fluctuating incidence which would be periodic were the value of r subsequently decreased in a regular manner. The second case of little or negative exaggeration, particularly marked when L is low, would result in very much less marked response to changes in either m or r and in a tendency to stabilization of L without fluctuation, oscillations being greatly dampened.

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A NOTE ON THE EPIDEMIOLOGY OF MALARIA

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A mathematical theory of the transmission of malaria has been presented by Macdonald (1952a, b), and the assumptions as to the nature of the disease and the rôle of the vector which he makes are retained here.

The present paper contains a derivation of the formula for the infection rate in mosquitoes, previously obtained by rather less formal methods by Macdonald (1952a), and an examination of the effect on the human infection rate of an increase in the anopheline density, which supplements the account given by Macdonald (1953, above).

Infection rate in mosquitoes

Suppose the probability of a mosquito surviving t days is e^{-vt}, so that, in Macdonald's notation, $p=e^{-v}$ and $v=-\log_e p$. Assuming that the mosquito population is stationary, births being balanced by deaths, the proportion of mosquitoes alive at any moment which were born between t and $t+dt$ days ago is

$$ve^{-vt}dt \quad .. \quad .. \quad .. \quad .. \quad .. \quad .. \quad (1)$$

Let n be the length of the extrinsic cycle, a the mean number of men bitten by one mosquito in a day, and x the proportion of people infected. Then, for $t>n$, a mosquito aged t days will have had $t-n$ days on which it might have fed on human beings, in order to be infective by the present time. The probability that in an interval of $t-n$ days a mosquito bites at least one infected person is

$$1-e^{-ax(t-n)} \quad .. \quad .. \quad .. \quad .. \quad .. \quad .. \quad (2)$$

The proportion of infected mosquitoes is, therefore, from (1) and (2),

$$s=\int_n^\infty ve^{-vt}\left\{1-e^{-ax(t-n)}\right\}dt$$

$$=\frac{axe^{-vn}}{ax+v}$$

$$=\frac{p^n ax}{ax-\log_e p} \quad .. \quad .. \quad .. \quad .. \quad .. \quad .. \quad (3)$$

This expression for the infection rate in mosquitoes is the same as that derived by Macdonald (1952a, p. 579) by a rather different method. In both derivations a constant value of x is assumed, but it would be reasonable to use this formula for s even if x were changing moderately, using the value of x which prevailed rather more than n days before.

Effect on human infection rate

Suppose a stable position has been achieved, with the human infection rate x_0, and the mosquito infection rate

$$s_0=\frac{p^n ax_0}{ax_0-\log_e p}.$$

In this equilibrium position the inoculation rate, h_o, is given by

$$h_o = m_o a b s_o, \quad .. \quad .. \quad .. \quad .. \quad .. \quad (4)$$

where, following the notation of MACDONALD (1952b, 1953), $m_o a$ is the mean number of mosquitoes biting a man daily, and bs_o is the proportion of them which are infective.

Further, MACDONALD (1950) has shown that, in the equilibrium position, $x_o = h_o/r$, r being the recovery rate, provided that $h_o < r$.

Suppose now that this equilibrium position has been achieved at time $t=0$, and that at the subsequent time $t=n$ days the inoculation rate is suddenly raised from h_o to h_1. Equations (3) and (4) show that this increase in h may be due to changes in m, a, b or p; we assume for convenience that it is due to an increase in the anopheline density from m_o to m_1, and that a, b and p remain unchanged.

Let i denote the sum of the length of the extrinsic cycle, n, and that of the incubation period in man. Then, at time $t=i$, the earlier increase in the inoculation rate will start to affect the human infection rate, which will increase according to the formula

$$x = \frac{h_1}{r} - \left(\frac{h_1}{r} - x_o\right) e^{-rt}, \quad .. \quad .. \quad .. \quad .. \quad (5)$$

provided that $h_1 < r$ (MACDONALD, 1950). For a further $i+n$ days this increase in x will have no effect on s. Then s will start to rise, and after a further $i-n$ days (that is, at time $t=2i$), the rise in s will start to affect the rise in x. Equation (5) therefore holds from $t=i$ to $t=2i$ (the interval called i_2 by MACDONALD, 1953).

The differential equation for x which starts to apply at $t=2i$ days is (following MACDONALD, 1950)

$$\frac{dx}{dt} = h(t) - rx, \quad .. \quad .. \quad .. \quad .. \quad .. \quad (6)$$

where, in the formula for the inoculation rate, $h(t)$, it will be a sufficiently good approximation to substitute the value of x prevailing at time $t-i$. From (4), (3) and (5), then,

$$h(t) = \frac{m_1 p^n a^2 b \left\{h_1/r - (h_1/r - x_o)\, e^{-r(t-i)}\right\}}{a\left\{h_1/r - (h_1/r - x_o)\, e^{-r(t-i)}\right\} - \log_e p} \quad .. \quad .. \quad .. \quad (7)$$

$$= \frac{A - Be^{-rt}}{C - e^{-rt}}, \text{ say,}$$

where $A = m_1 h_1 a b p^n e^{-ir}/(h_1 - rx_o)$,

$B = m_1 a b p^n$,

and $C = (ah_1 - r \log_e p)\, e^{-ir}/a(h_1 - rx_o)$

Writing the differential equation (5) as

$$\frac{dx}{dt} = \frac{A - Be^{-rt}}{C - e^{-rt}} - rx$$

and integrating, we find that

$$x = \frac{A}{Cr} + \left\{K + \frac{(A - BC)}{C^2}\, t\right\} e^{-rt} + \frac{A - BC}{C^2 r}\, e^{-rt} \log_e (C - e^{-rt}), \quad .. \quad (8)$$

where K is a constant to be determined by the value of x at time $t=2i$. By (5), this value is

$$h_1/r - (h_1/r - x_o)e^{-2ir} = X, \text{ say.}$$

Substituting for K in (8) in the usual way, we obtain the final formula for x, valid for $t=2i$ to $3i$ (Macdonald's interval i_3):

$$x = Xe^{-r(t-2i)} + (A/Cr)\left\{1-e^{-r(t-2i)}\right\} + \left\{(A-BC)/C^2\right\}(t-2i)\,e^{-ir} + \left\{(A-BC)/C^2r\right\}e^{-rt}\log_e\left\{(C-e^{-rt})/(C-e^{-2ir})\right\} \quad \ldots \quad (9)$$

Equation (9) corresponds to the rather more approximate formula (11) of MACDONALD (1953), in the derivation of which a mean value for x over the period $(i, 2i)$ is used instead of the increasing value given by (5). The present method could theoretically be extended for subsequent time intervals of length i, but the algebra would rapidly become unmanageable.

The asymptote of (9), obtained by putting $t=\infty$, is

$$\frac{A}{Cr} = \frac{m_1h_1a^2bp^n}{(ah_1 - r\log_e p)r} = \frac{m_1ab\left\{s\,(h_1/r)\right\}}{r}, \quad \ldots \quad (10)$$

where $s\,(h_1/r)$ is the value of s given by (3) when $x=h_1/r$. This is greater than the original asymptote

$$h_1/r = \frac{m_1ab\left\{s(x_0)\right\}}{r},$$

since s is an increasing function of x, and $h_1/r > x_0$. The asymptote (10) is, however, never attained, because equation (9) holds only up to $t=3i$, after which time a new differential equation must be written for x.

The asymptote $x(\infty)$ of the whole process can easily be found, for it occurs when $dx/dt=0$, *i.e.*, when

$$h(\infty) = rx(\infty).$$

From (4) and (3),

$$h(\infty) = \frac{m_1a^2bp^nx(\infty)}{ax(\infty) - \log_e p.}$$

Eliminating $h(\infty)$ from these two equations, we find

$$x(\infty) = \frac{m_1a^2bp^n + r\log_e p}{ar}, \quad \ldots \quad (11)$$

which is the same expression as that developed by MACDONALD (1952b, equation (15)) for the equilibrium level of x. After a sufficiently large number of incubation periods of length i, therefore, the human infection rate x will have risen from its original stable level x to its new stable level given by (11).

Equation (11) clearly holds only if $x(\infty) \leq 1$, that is if

$$m_1a^2bp^n + r\log_e p \leq ar,$$

$$\text{or} \quad r \geq \frac{m_1a^2bp^n}{a - \log_e p},$$

that is, if r is greater than or equal to the highest value of h that can possibly occur (putting $x=1$ in (3)). If, on the contrary,

$$r < \frac{m_1a^2bp^n}{a - \log_e p},$$

then at some stage during the whole process h becomes bigger than r, and the second form of the differential equation for x must be invoked (see MACDONALD, 1950).

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SUMMARY OF RECENT ABSTRACTS*

VIII. TYPHUS GROUP OF FEVERS

General

A quantitative estimation of rickettsial antigens in infected yolk sac membranes, by means of a complement-fixation test in which 50 per cent. haemolysis technique was used, is described by Boyd (p. 32). Residues from the manufacture of antibiotics are used as growth promoters by chicken farmers, but Greiff and Pinkerton (p. 609) found that eggs from such hens would not support the growth of rickettsiae. Eggs for culture work, therefore, should not be from hens fed in this way.

Neva and Snyder (p. 1106) show that the white rat, like the white mouse, is susceptible to the toxic action of living typhus rickettsiae (of murine, epidemic or Rocky Mountain fever type) injected intravenously.

A test of therapeutic efficiency in rabbits of aureomycin, chloramphenicol and streptomycin, which depends on the power of these substances to neutralize rickettsiae of murine or epidemic typhus injected at the same spot as the antibiotics, or even at a different place, is described by Giroud and Ciaccio (p. 32). Weyer (p. 255) used lice in tests of the activity of antibiotics on rickettsiae, inoculating them intrarectally with suspensions exposed to the drugs *in vitro* for various periods, and subsequently examining smears of the gut. Aureomycin and terramycin [oxytetracycline] were rickettsiocidal in the dilutions used, but chloramphenicol was rickettsiostatic on *R. prowazeki* and *R. quintana* and had no effect on *R. rickettsi*. None of them had any effect on *R. burneti* (tested by inoculation of white mice). Studies on respiration of murine and epidemic typhus rickettsiae *in vitro* under the influence of antibiotics similarly indicate that aureomycin and terramycin are rickettsiocidal, and that chloramphenicol (presumably) has little or no action of this kind (Karp and Snyder, p. 763).

Proteus OX19 type: Vectors louse and flea

Louse typhus

In Turkey, Onul (p. 609) has observed laboratory infections with typhus in which the Weil-Felix reactions were at unusually low titres, perhaps because of previous inoculation.

Diseases of the typhus group are rare in the Sudan. Drysdale and Kirk (p. 679) report two from one compound. One of them gave a reaction with *Proteus OX19*, and there was no eschar, but in comment Megaw points out that these features do not with certainty rule out the diagnosis of tick typhus.

Da Rocha Lima (p. 131) has published a paper on the discovery of *R. prowazeki*.

Typhus fever in 3 patients apparently contracted through blood transfusion from a healthy donor, whose Weil-Felix test was subsequently found to be positive, is described by Kimura (p. 133), who thinks that the donor was a healthy carrier, and that his blood was intermittently positive.

Giroud and Gaillard (pp. 680, 1035) passaged *R. prowazeki* intrarectally in lice, but found that the strain tended to die out in later passages. They

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1952, v. 49. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

postulate the development of a lytic agent, and relate this happening to the wane of natural epidemics in man.

Kryński and his colleagues (pp. 680, 763) have made a study of lice feeding on guineapig blood, which they suck readily but which they do not utilize for nourishment. Death of lice fed on guineapig blood is due to mechanical injury to the intestine resulting from crystallization of the haemoglobin. Kryński (p. 763) shows that the best blood meals for lice are provided by persons whose haemoglobin levels are high and who are well nourished.

Crab lice are potential vectors of louse-borne typhus, but their habit of remaining persistently attached to the same host deprives them of any great significance in transmitting the disease. Weyer (p. 762) shows that head lice are as susceptible as body lice. He (p. 1036) also shows that the hog louse *Haematopinus suis* can be infected with *R. prowazeki*.

Brill's disease, regarded as a late relapse of epidemic typhus years after the initial attack, has attracted much attention. Cases have been reported as follows:—Worms *et al.* (p. 383) in Paris; Löffler and Mooser (p. 762) in Switzerland; Becker and Kaether (p. 763), Binde *et al.* (p. 497) and Willsch (p. 609) in Germany; Murray *et al.* (p. 383) in Yugoslavia; Gear *et al.* (p. 1107) in South Africa; Murray *et al.* (p. 681) and Sigel *et al.* (p. 762) in the United States. These patients had usually lived long ago in the endemic areas of Europe and had experienced no attack since the first, many years earlier. In most cases reinfection was not possible and the disease appeared to be a true late relapse, with positive complement-fixation or rickettsia-agglutination tests. Weyer (p. 1036) thinks that from such patients lice may pick up the infection to start new epidemics, and Gear *et al.* (p. 1107) are of the same opinion. They think that treatment with antibiotics will not prevent the survival of rickettsiae, and that a community which has had an epidemic of typhus remains a potential reservoir for the lifetime of the infected generation. In a comment on the paper by Willsch, Megaw supports the view that antibiotics, whose action is rickettsiostatic, may not eradicate the infection, citing the parallel instance of scrub typhus, in which early treatment with antibiotics is often followed by early relapse. Early treatment seems to interfere with the development of solid immunity. [See, however, Smadel *et al.* in the section *Proteus OXK type*: *Vector mite*, below.] Similarly, Siegert (p. 385), who reports a study of the action of aureomycin against *R. prowazeki in vitro* and in guineapigs, states that the later treatment was started the higher the degree of immunity developed. Successful treatment of typhus in Cairo is reported by Killough and Magill (p. 497); they gave terramycin in doses of 75 mgm. per kgm. every 4 hours.

The official standards required for typhus vaccines in Germany are discussed by Otto (p. 385).

Experimental work by Wojciechowski (p. 384) in guineapigs indicates that a vaccine of *R. prowazeki* from mouse-lung preparations did not protect against 200 infecting doses, whereas vaccines from louse guts and yolk sacs of hen's eggs gave good protection, especially if the rickettsiae were treated with ether. In the State Institute of Hygiene, Crakow, where all the members of the staff had been immunized against typhus, rickettsia-agglutination and Weil-Felix tests were highest in those in constant contact with rickettsiae, and in those on whom lice fed (Ulewicz, p. 132).

Gauld and Goodner (p. 33) gave a dose of a typhus vaccine to men who had been immunized several years previously; even after this long interval the response, as judged by complement-fixation, neutralization and rickettsia-agglutination tests, was good. Prompt response to late booster

doses of typhus vaccines was also observed by Murray *et al.* (p. 610) in a number of persons who had been immunized 4–6 years previously.

Rickettsiae other than *R. prowazeki* were found in lice fed on patients recovering from typhus and typhus-like fevers in Peking. Liu and Landauer (p. 939) found them antigenically distinct from *R. prowazeki*, and they discuss their identity.

Flea typhus

Rickettsial diseases, especially flea-borne typhus, occur in Sicily, and their incidence is discussed by Castorina (p. 31).

Giroud (p. 383) has summed up much of his work on the rickettsial diseases of French Equatorial Africa. He and his colleagues (p. 1036) have found severe disease of murine type, and think that diagnosis can be facilitated by electrophoretic methods. Giroud and Grjebine (p. 254) discuss the rickettsial diseases of the Middle Congo, and conclude that only two are found, namely murine typhus and boutonneuse fever.

Kalra and Rao (p. 939) have investigated the typhus fevers of Srinagar, Kashmir, and report a considerable number of cases of the murine type, with high incidence in spring and summer. This murine form is apparently more prevalent than the epidemic form, but the authors think that the lice may play a part in transmission. They (p. 940) found typhus of murine type in Bangalore and Mysore, and refer to the former finding of a fever of the Rocky Mountain spotted fever type there.

Small outbreaks of flea-borne typhus occur in various parts of Japan, and Kitaoka *et al.* (p. 610) describe several, with comments on the value of the complement-fixation and rickettsia-agglutination tests for diagnosis from louse-borne typhus.

Murine typhus rickettsiae can be isolated from the blood and brain of infected guineapigs as early as 10 minutes after intraperitoneal infection, and the animals remain in this state of inapparent infection throughout the incubation period (Noury, p. 134).

In Texas Davis (p. 497) found that *Xenopsylla cheopis* and *Leptopsylla segnis* were the two commonest fleas on rats (especially *Rattus norvegicus*), the latter being most prevalent in spring. The season of prevalence of flea-borne typhus (July–October) follows 2 months after the rise in numbers of *X. cheopis*.

In a study of metabolism of rickettsiae of murine typhus Wisseman and his colleagues (pp. 134, 681) found a rough correlation between the nitrogen content of a purified suspension and the amount of complement-fixing antigen, toxin titre and rate of oxidation of glutamate. The last was not affected by chloramphenicol, aureomycin or terramycin, but was affected by enzyme inhibitors. They have studied the oxidation of glutamate by *R. mooseri*.

Suzuki (p. 764) has extracted a toxoid-like substance from *R. mooseri* by freezing and thawing and by supersonic irradiation.

Experimental work with a murine antigen suggests that animals on diets deficient in pyridoxine, riboflavin or folic acid do not develop complement-fixing antibodies after infection to the same extent as controls, but Wertman *et al.* (pp. 256, 1107) show that an inanition diet, or a diet deficient in nicotinic acid, makes little difference.

Morlan and Hines (p. 34) show that control of murine typhus in southern U.S.A. by a wide programme of dusting with DDT has remained effective for 3 years, though the numbers of *X. cheopis* and rats, which had sharply declined soon after the programme was started, began to increase 6 months after the end of the operation, but did not reach the former levels.

Proteus OXK type: Vector mite

Kalra and Rao (p. 939) have encountered scrub typhus in Kashmir, where *Trombicula deliensis* is found.

Audy *et al.* (p. 135) describe Jarak Island, in the Straits of Malacca, of which they made a survey, partly for scrub typhus.

Munro-Faure *et al.* (p. 256) report two cases of scrub typhus in British soldiers in Korea; probably the first cases to be recorded.

Fukuzumi *et al.* (p. 34) in Japan found *R. tsutsugamushi* in the field mouse *Apodemus speciosus speciosus*. They claim that *Trombicula pallida* can transmit the infection.

A long monograph on the scrub-typhus mites of the Asiatic-Pacific region has been prepared by Womersley (p. 942).

Harrison and Audy (p. 764) have published a check-list of recorded hosts of *Trombicula akamushi* and *T. deliensis* (which they regard as belonging to a single species or species-complex). The principal hosts are field-dwelling varieties of *Rattus rattus* and the conditions for abundant propagation of this species are created by man when he removes the forest canopy and grows food crops.

From their own work and from a study of the literature Bailey *et al.* (p. 34) conclude that chloramphenicol is the drug of choice for scrub typhus, though aureomycin and terramycin are almost as good. For *R. rickettsi* and *R. tsutsugamushi* in embryonated eggs the most active antibiotics were found by Jackson (p. 137) to be terramycin, aureomycin and chloramphenicol.

In a detailed investigation of immunization with lyophilized live yolk-sac vaccines against scrub typhus, followed by treatment with chloramphenicol, Smadel *et al.* (p. 682) show that a high degree of immunity develops against the homologous strain even when the disease is suppressed by chemotherapy, but that the immunity against heterologous strains is short-lived and incomplete.

When mice are immunized with *R. tsutsugamushi* of low virulence they become highly resistant to a strongly virulent strain in 20 days, but Kuwata (p. 611) points out that the superinfecting organisms persist for long periods in their tissues. The same is true if the immunizing strain is virulent. It is not clear why highly resistant mice cannot eliminate these persisting rickettsiae.

In a riverine area of Japan notorious for scrub typhus, in which attempts at control by immunization had failed, Kitaoka *et al.* (p. 257) succeeded in protecting the working population by issuing a 6 per cent. emulsion of benzyl benzoate three times during the season June–September for impregnation of clothing, and dimethyl phthalate for application to the skin. They treated the disease successfully with chloramphenicol.

Indeterminate type: Vector tick

Perepérez Palau (p. 853) reports a fever, probably tick-borne of the boutonneuse type, in Tarragon, Spain.

Strains of boutonneuse fever were isolated from *Rhipicephalus sanguineus* taken from dogs in the Crimea by Korshunova and Petrova-Piontkovskaya (p. 765).

Most cases of tick-bite fever in Africa are seen in Europeans, but Gelfand (p. 611) now reports one in an African. He suggests that African children may become infected but that the symptoms may be so mild in them that they are not brought to hospital.

In French Equatorial Africa mouse-protection and agglutination tests with *R. prowazeki* and *R. mooseri* have been found positive in patients with boutonneuse fever, and in healthy cattle. Giroud *et al.* (p. 1106) regard this as suggesting that domestic animals may be reservoirs of boutonneuse fever or epidemic typhus, or that the specificity of the antigens may not be absolute. Tick-borne typhus is reported by Baussay (p. 853) from Oubangui, French Equatorial Africa.

Philip (p. 765) reports on the recovery of a strain of tick-typhus rickettsia from ticks in India, and its relationship to the rickettsia of boutonneuse fever. In comment Megaw remarks on the fact that the tick-borne typhus fevers are as closely related to each other as the varieties of mite-borne scrub typhus. Philip and Kohls (p. 498) think that a case of Rocky Mountain spotted fever may have been acquired from a tick (probably *Dermacentor albipictus*) from an elk, which attached itself to the person who was skinning the animal. It is not known where the tick acquired its infection.

A few cases of Rocky Mountain spotted fever have been reported from Alberta, Canada (Bow and Brown, p. 766).

Silva-Goytia and Elizondo (p. 1037) claim to have found evidence of the existence of the rickettsiae of Mexican spotted fever in human lice and to have isolated them from various ticks.

Calero *et al.* (p. 1108) have recognized Rocky Mountain spotted fever in Panama.

Excellent results in the treatment of Rocky Mountain spotted fever with chloramphenicol and cortisone are reported by Workman *et al.* (p. 1037), but they do not advise this as a routine until further experience has been gained.

Q Fever

Q fever has attracted a great deal of attention recently, and has now been found in most parts of the world. It is endemic all over Switzerland and the neighbouring territories, and Wiesmann (p. 766) shows that 1,080 cases were diagnosed by the complement-fixation test in just over 4 years. Lass (p. 612) has observed 360 cases in Austria within a few years. It is important in Italy, and has been confirmed in 13 of the 20 provinces. A conference reported in *Ann. d. San. Pubblica* (p. 1038) suggested, among other things, the standardization of the complement-fixation test, which is the most useful method of diagnosis. Di Marco and d'Agata (p. 258) describe 2 cases from Catania, Italy.

An explosive outbreak in men of a U.S.A. Air Force unit in Tripoli is described by Fellers (p. 613). Radiological evidence of pneumonitis was common.

Harris (p. 853) reports the disease from Nairobi, Kenya.

Positive complement-fixation tests were found in Ceylon by Schmid *et al.* (p. 1109) in slaughter-house workers and in various domestic animals, and in 4·6 per cent. of residents examined in Quebec by Pavilanis *et al.* (p. 766).

There has been much evidence that domestic animals are the reservoirs of infection, and cattle, sheep and goats have usually been incriminated. In Germany Schubothe *et al.* (p. 36) relate an outbreak to flocks of sheep brought from mountain pastures each year, and in the island of Lipari Lopes (p. 499) similarly attributes an outbreak to flocks of goats driven daily through the streets; many of the goats gave positive complement-fixation tests, and there was serological evidence of many sub-clinical attacks in the people. The disease is widespread in cattle, sheep and goats

in Portugal (Fonseca and Pinto, p. 258), Egypt (Halawani *et al.*, p. 1038), and in Iran (Giroud and Yassemi, p. 683).

Clark *et al.* (p. 38) refer to the well-known "goat-boat fever" of California in the crews of Californian ships carrying goats. Infection may be due to infected milk or dust. Lennette and Welsh (p. 38) in the same area found *R. burneti* in the air of a goat milking shed. Another outbreak in California may have been due to infected dust, and Clark *et al.* (p. 38) found evidence of infection in flocks of sheep in the neighbourhood.

In North California Q fever is chiefly acquired from sheep, in the months March–May when lambing, castration and docking processes are undertaken. Lennette *et al.* (p. 39) and Clark *et al.* (p. 258) show that in South California, where cattle are the chief source of infection, no such seasonal prevalence is observed. Most of the patients in North California are males in contact with live-stock and the mode of infection is probably by inhalation of infected dust or droplets. Complement-fixation tests indicate that there must be many inapparent infections.

After intravenous injection of *R. burneti* in sheep, the animals showed little sign of illness and the antibody response was varied. Lennette *et al.* (p. 767) found that nasal and mammary secretions were only very rarely infective in these animals, and urine, faeces and oral secretions were never found positive. At autopsy the sheep were in excellent condition but rickettsiae were recovered in pooled organs and in a few lesions in some of them. *R. burneti* has been found by Welsh *et al.* (p. 386) in the placentas of naturally infected sheep in California.

In Texas Irons *et al.* (p. 499) found positive complement-fixation tests in the pack rat *Neotoma micropus*. They found *R. burneti* in the milk of 2 cows in one dairy.

Babudieri and Moscovici (p. 612) have found some evidence that pigeons from areas where Q fever occurs may play an important part in transmission because of their habit of feeding on the droppings of mammals. Certain pigeons could be experimentally infected by the oral route, and the kidneys of one so infected were apparently infective several months later.

Inhalation of infected dust is a very common means of infection. For instance, the outbreak at a college of art in Kent was associated with dust from a packing case which contained wood shavings, paper and mouldy straw, and which was opened after having been kept for some years (Harvey *et al.* p. 385). Dust from maize grain used for feeding cattle was proved to be infected by Bingel *et al.* (p. 1109), and dust from the operation of threshing was suspected by Murray *et al.* (p. 37) and Šimović *et al.* (p. 37).

An outbreak of Q fever in students at an agricultural college in California was thought to be due to inhalation of infected dust, though Clark *et al.* (p. 38) could not be sure of the mode of infection. Many of the patients (but not all) had been in contact with sheep.

The morphology of *R. burneti* is described by Kausche and Sheris (p. 135).

Ormsbee (p. 612) shows that in embryonated eggs, growth of *R. burneti* is restricted to the yolk sac, and that multiplication ceases on death of the embryo.

Blanc *et al.* (p. 259) have shown that *R. burneti* can survive in *Trombicula autumnalis* for 24–54 hours, but it is not certain that they can multiply.

Kirberger (p. 39) tested suspensions of *R. burneti* for susceptibility to heat and to various disinfectants. For hot-air disinfections a temperature of 70°C. is needed, for clothing the disinfectant Sagrotan is recommended, and for the skin 70 per cent. alcohol is suitable. Lennette *et al.* (p. 766) tested the survival of *R. burneti* in milk after pasteurization, and found a few specimens in which it persisted after the holder process or the HTST

method, although higher temperatures or longer periods, or both, were employed than are required by the California regulations.

The nucleic acids of *R. burneti* have been studied by Smith and Stoker (p. 259).

Siegert *et al.* (p. 499) prepare antigens for diagnosis of Q fever from the Henzerling and Zurich strains of *R. burneti*, with good and equal potency. Herzberg *et al.* (p. 500) show by experimental work in guineapigs that certain Mediterranean strains of *R. burneti* differ considerably from certain South-German strains in their complement-fixing and agglutinating antigens.

Ormsbee (p. 502) reports the biochemical changes which occur in milk after injection of *R. burneti* into the udders of cows. In testing whey from the milk of cows whose sera gave positive reactions with the complement-fixation test for *R. burneti*, Stoker and Marmion (p. 683) found that the direct agglutination test was much more sensitive than the fixation test, especially when the rickettsiae were centrifuged and re-suspended in saline or normal serum. This test would be suitable for a preliminary survey of suspected herds.

A slide-agglutination test for Q fever is described by Haas (p. 501).

After investigating 102 patients with Q fever, Lennette *et al.* (p. 1039) find that the rickettsia-agglutination test has some advantages over the complement-fixation test for early diagnosis, but that the latter is more readily adaptable to laboratory use. Both are very good, and the antibodies persist for a long time, which indicates the need for caution in diagnosis unless repeated tests are carried out. Herzberg *et al.* (p. 40) show that the rickettsia-agglutinating antigens of Q fever in Europe are as variable as the complement-fixing antigens have been shown to be. There is no uniform correlation between them, and the authors conclude that these tests sometimes give results which raise doubts as to their specificity. The complement-fixation test can be used to measure the infectiousness of suspensions of *R. burneti* and also, presumably, the potency of vaccines (Ormsbee *et al.*, p. 259).

Lennette *et al.* (p. 500) have shown that brucellosis and syphilis do not apparently lead to false positive tests for Q fever, but that a false positive syphilis test may appear in the course of Q fever.

Victor *et al.* (p. 501) have devised a method for determining the opsonins for *Brucella*, and have shown that these may enormously increase in brucellosis. They have now applied a similar technique to Q fever, and they find that this test is a very sensitive indicator of infection, and that few false positive results occur. The technique may need a high degree of technical skill, though it is claimed to be convenient and easy.

Babudieri and Ravaioli (p. 260) show that the Giroud skin test in Q fever in guineapigs did not become positive until the sixteenth day, whereas the complement-fixation test was usually positive on the seventh.

Steinmann (p. 136) describes certain granules and filaments in macrophage cells in the sputum in Q fever, which may be valuable in diagnosis.

Clark *et al.* (p. 136) describe the clinical features in 180 cases of Q fever in which, although there were no deaths, the disease was comparatively severe. Onset was usually sudden, with rigor and headache; cough and signs in the chest were found in about one-quarter. Duration of fever was about 12·5 days and there was little response to aureomycin. The rickettsia-agglutination or the complement-fixation test was positive in all cases.

In Q fever the dominating radiological feature is a circumscribed, usually rounded, lesion of exudative-pneumonic character; Glücker and Munk (p. 1039) discuss the differential diagnosis from this point of view.

Ormsbee and Pickens (p. 613) tested the effect of terramycin, aureomycin and chloramphenicol against *R. burneti* in embryonated eggs, the antibiotics being injected into the yolk sac 24 hours after infection, and results being calculated on the complement-fixing units per mgm. nitrogen. Effectiveness was in that order, and all were more useful than penicillin G. From an experience of 25 cases Fellers (p. 853) concludes that both aureomycin and chloramphenicol produce a dramatic therapeutic response in Q fever. This, however, is not the conclusion reached by Clark *et al.* (p. 136) in severely affected patients.

After a field experiment, Luoto *et al.* (p. 767) conclude that there is a possibility that a killed vaccine may be useful in the control of Q fever in dairy cattle.

Rickettsialpox

Le Gac and his colleagues (pp. 35, 256) claim that rickettsialpox has been found in a few patients in French Equatorial Africa, basing their diagnosis on the fact that the serum of guineapigs injected with the blood of the patients agglutinated *R. akari* to a titre of 1 in 20, or on agglutination by serum from a patient. They describe (p. 498) the eschar which occurs in this disease. The histology of this eschar is closely related to that of boutonneuse fever, with which the disease has antigenic affinities. In describing a later explosive outbreak these authors (p. 682) refer to it as African varicelliform rickettsiosis. Of 12 patients 4 died, and in 5 of the remainder the agglutination test against *R. akari* was positive; in 7 the test was positive against *R. burneti.*

In the United States Fuller *et al.* (p. 35) succeeded in isolating *R. akari* from mice trapped in the place of employment of a woman who had had rickettsialpox. They describe the techniques used, and they conclude that this infection may be expected wherever the mite *Allodermanyssus sanguineus* and house mice occur in association with each other. They did not obtain confirmation of the view that *R. akari* is closely related to the antigens of Rocky Mountain spotted fever.

Eustis and Fuller (p. 1108) in the United States have isolated *R. akari* from mites (*A. sanguineus*) collected from the walls of incinerators in a house in which rickettsialpox had occurred. *Charles Wilcocks*

MALARIA

Young, M. D. **Malaria during the Last Decade.** *Amer. J. Trop. Med. & Hyg.* 1953, May, v. 2, No. 3, 347–59. [Numerous refs.]

The author reviews those happenings in the field of research on human malaria during the last 10 years which appear to him to be particularly significant. His article is itself a very compact summary not susceptible to further compression, but the subject headings can indicate the scope and it is interesting to see how great the progress in this time has been and which developments he appears to think of most significance. The headings are: Biology; Immunology; Culture; Diagnosis; Vectors; Chemotherapy; Control; Incidence and Methodology. The discovery of the exoerythrocytic cycle is almost complete though the potentialities of research which it opens, particularly by tissue culture, are almost undeveloped. The author clearly sees much epidemiological significance in

studies of homologous and heterologous immunity stimulated by different species of parasite, of their natural persistence in the body, and in studies of anopheline susceptibility through the production of hybrid strains.

The full study of existing synthetic antimalarial drugs and the development of new ones has shown great progress; among the most promising developments is the recent demonstration of the value of primaquine as a non-toxic cure for relapsing *Plasmodium vivax* infections. The production of parasite resistance to some is disquieting but has not yet been demonstrated in the case of quinine, chloroquine or quinacrine [mepacrine] [but see Fairley, this *Bulletin*, 1947, v. 44, 399]. The possibility of anopheline resistance to insecticides is also disturbing, and its production by the use of larvicides well established. These forms of resistance to new remedies emphasize the need for continuing research to maintain our present advantage, but the developments in research method have been so great that it is justifiable to be optimistic about the prospects of success for the WHO ambition to eliminate malaria as a public health problem from the world.

[This review is interesting, well documented and valuable. Workers on any aspect of malaria could read it with both pleasure and profit.]

G. Macdonald

Bruce-Chwatt, L. J. **A Diagram of the Epidemiology of Malaria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1953, Mar., v. 47, No. 2, 166–8, 1 diagram.

When the needs of teaching include a diagram of the chain of transmission it is usual to employ one connecting man-mosquito-man, and omitting reference to environment. The author presents a new diagram of the relationship of epidemiological factors which include environment. The parasite and the vector are linked together as the agent of disease, and tied to a representation of the physical, biological and socio-economic environment.

[The diagram provides a better background for teaching than does the usual one, and should be seen in the original by those teaching the epidemiology of malaria.]

G. Macdonald

Holstein, M. Enquêtes épidémiologiques sur le paludisme dans le cercle de Bobo-Dioulasso (Haute-Volta, 1949–1950). [**Epidemiological Study of Malaria in the Bobo-Dioulasso Area**] *Acta Tropica*. Basle. 1953, v. 10, No. 2, 113–25.

This paper on malaria in the Haute Volta extends that published by Jonchère and Pfister [this *Bulletin*, 1952, v. 49, 590], recording the results of 56 sample surveys in locations in the Cercle de Bobo-Dioulasso, and 2 in Bobo itself. The human material was mainly children not in receipt of prophylactic drugs. Spleen rates, degrees of enlargement, parasite rates, gametocyte rates, and combined spleen and parasite rates are given for each survey. Taken together they show moderate endemicity with occasional hyperendemic areas, *Plasmodium falciparum* predominating over *P. vivax* and *P. malariae*, the last being rare except in Banfora, a much irrigated and holo-endemic area.

The anopheline fauna includes *Anopheles gambiae*, *A. funestus*, *A. rufipes*, *A. nili*, *A. pharoensis*, *A. squamosus*, *A. brunnipes*, *A. domicolus*, *A. hancocki*, *A. flavicosta* and *A. pretoriensis*, the first 3 being notable vectors showing sporozoite rates within the following ranges: *A. gambiae*

3·1 to 13·2 per cent., *A. funestus* 2·7 to 9·0 per cent. and *A. rufipes* 3·5 to 8·4 per cent. Of these 3, *A. funestus* is much the most numerous and therefore the most important vector; *A. gambiae* is subsidiary to it in most places though not in Bobo itself. It is stressed that *A. rufipes* must be counted as an important carrier; though it constitutes only 1·64 per cent. of the captured anopheline fauna, it showed a mean sporozoite rate of 7·4 per cent. *G. Macdonald*

Friedmann, M. **Malaria Infection limited to certain Families.** *Documenta Med. Geograph. et Trop.* Amsterdam. 1953, Mar., v. 5, No. 1, 72–4.

In North Holland some houses are particularly attractive to mosquitoes and there is a high prevalence of malaria in them. House epidemics also occur in the Shevaroy Hills of South India; malaria is transmitted by *A. fluviatilis* and is locally rare, the spleen rate being 8 per cent. Six examples of house epidemics in Yercand, South India, are quoted in each of which a number of people living in one house suffered simultaneously from an attack of malaria due to the same species of parasite. The examples include houses of well-to-do and poor families and there is no reason to suppose that they were peculiarly attractive to anophelines. It is suggested that *A. fluviatilis* may bite 4 or 5 times a night with the consequence that a single infected mosquito produces a house epidemic. *G. Macdonald*

Fritz, R. F. & Andrews, J. M. **Imported and Indigenous Malaria in the United States, 1952.** *Amer. J. Trop. Med. & Hyg.* 1953, May, v. 2, No. 3, 445–56, 3 figs. [15 refs.]

The decline and fall of malaria in the U.S.A. is almost complete. It was basically a natural process [this *Bulletin*, 1946, v. 43, 286; 1949, v. 46, 111] accelerated by deliberate design [*ibid.*, 1949, v. 46, 440], and documented step by step [*ibid.*, 1950, v. 47, 815; 1951, v. 48, 430]. The present paper describes the last struggles, the scale of which may be judged from the fact that case histories are given for more than half of the known fresh indigenous malarial infections occurring in the U.S.A. in the course of a year. They are 25 in number; the total of cases is thought to be 47, of which 32 are established and 15 presumed.

The story is complicated by the return of many soldiers infected in Korea and by the continued notification of cases, the enormous majority of which are not substantiated on enquiry. Korean cases are all due to *Plasmodium vivax* and show a pattern of relapse similar to that generally seen in temperate countries; long latency is common and initial attacks are most frequent in the months of May and June. Though numerous it seems that they have produced very few secondary indigenous cases.

The Federal control programme is no longer based on general anti-mosquito work, but on the detailed investigation of suspected cases and the design and execution of special schemes around each. The return of veterans and the appearance of even a few secondary cases around them have presented difficult problems but have not materially altered the prospects of eradication of the disease from the States. *G. Macdonald*

then begun in the 3 different hosts. Incidentally, the authors find it difficult to accept mutation as an explanation of the stepwise development of resistance in these organisms.

Intraperitoneal inoculation with a known number of trypanosomes was adopted to produce infection in rats of approximately 200 gm., mice of 15 to 18 gm., and guineapigs of 200 to 220gm. The degree of infection was followed in fresh preparations of blood, and numbers of trypanosomes present were recorded arbitrarily. Even when the same number of trypanosomes were given it was found that the average period of survival in all 3 hosts was longer when they were infected with the resistant strain than with the normal strain, and was associated with a longer prepatent period in the former.

Infections were of two types: (1) a progressive type leading to death of the host, (2) a relapsing type with increase and decrease in the numbers of trypanosomes till death of the host finally resulted from an upsurge of infection. In mice the progressive type of infection, and in guineapigs the relapsing type, invariably occurred. In the case of 45 rats which received inocula of different sizes of the normal strain only the progressive type of infection resulted, whereas of 49 rats inoculated with the resistant strain, 14 exhibited a progressive infection and the remainder an infection of relapsing type, suggesting that immune reactions are involved. Detailed analysis showed that the time taken from the occurrence of a relapse to the death of a host was the same as that occurring in a progressive infection, or in other words the relapse strain killed the rats in the same time as a normal strain.

The explanations put forward of the change in the pattern of infection as the result of development of arsenic resistance are that the resistant strain may multiply less rapidly and produce toxic material in smaller amount than the normal strain, or that different metabolic products are produced with alteration in the immune responses of the host. *J. D. Fulton*

Cantrell, W. **The Effect of Mapharsen on the Glucose Metabolism of** *Trypanosoma equiperdum*. *J. Infect. Dis.* 1953, Mar.–Apr., v. 92, No. 2, 191–4. [10 refs.]

It has been suggested by previous workers that arsenicals such as mapharsen (*m*-amino-*p*-hydroxy phenyl arsenoxide) and phenylarsenoxide [this *Bulletin*, 1948, v. 45, 495, 773] interfere with glycolytic reactions of trypanosomes. In this investigation experiments were made with *T. equiperdum* from mapharsen-treated rats to find whether less glucose is used and less pyruvic acid produced by them than by normal trypanosomes. When a rat with approximately 10^5 trypanosomes per cmm. blood was treated intravenously with 0·516 mgm. mapharsen per kgm., about 10 per cent. of the parasites disappeared in 45 minutes, and about 90 per cent. in 108 minutes. Infected blood was therefore isolated just before trypanosomes began to disappear and their consumption of glucose was measured at the same time as that of normal trypanosomes from a similarly infected control rat, due allowance being made for the fact that rat blood is glycolytic.

It was found that treated and untreated trypanosomes used the same amount of glucose, suggesting that mapharsen does not act primarily by interference with the glycolytic process. The amount of pyruvate produced by treated trypanosomes was about 82 per cent. of that in untreated. The author is of the opinion that his data exclude the probability that mapharsen acts on hexokinase, but it may act at a later stage in the glycolytic system or possibly on some other metabolic system. *J. D. Fulton*

McRary, W. L., Beaver, E. L. & Noble, E. R. *In Vitro* **Effects of Prodigiosin and other Antibiotics on** *Trypanosoma cruzi*. *Exper. Parasit.* New York. 1953, Apr., v. 2, No. 2, 125–8. [11 refs.]

For the study of the *in vitro* effect of 9 antibiotics (aureomycin, bacitracin, chloramphenicol, fumagillin, neomycin, polymyxin B, prodigiosin, subtilin and terramycin) upon *Trypanosoma cruzi*, cultures of the latter, grown on Little and Subbarow's medium [this *Bulletin*, 1946, v. 43, 538], were suspended in glucose-salt-peptone solution (about 12 million flagellates per ml.), to which the antibiotic solutions were added in concentrations from 1 to 1,000 μgm./ml. The results—which are shown in 2 tables—were assessed by the degree of inhibition of growth, determined by counting the number of motile flagellates per high power field.

Of all the antibiotics tested, prodigiosin and polymyxin B proved to be the most effective, the former inhibiting 100 per cent. organisms at concentrations from 10 to 25 μgm./ml. in 30 minutes and at 1 μgm./ml. in 48 hours, while the effect of the latter drug at 100 μgm./ml. is manifested only after several hours. Tests with a mixture of the two antibiotics revealed no synergic action. *C. A. Hoare*

Haron, T. Inquérito epidemiológico e profilaxia da Moléstia de Chagas no município de Garça, Estado de São Paulo. [**Epidemiological Study and Control of Chagas's Disease in Garça, São Paulo**] *Arquivos de Hig. e Saúde Pública*. S. Paulo. 1952, Mar., v. 17, No. 51, 15–25. English summary.

The English summary appended to the paper is as follows:—

"It was demonstrated that the wettable powder of BHC, varying from 0·10 g to 0·50 g per square meter sprayed on wood, brick and mud walls has a good action against nymphs and adults of *Triatoma infestans* vector of Chagas' Disease in Garça, a town of the State of São Paulo, Brazil.

"After the 75th day of the spraying, specimens dead or alive of the insect, were not found.

"The BHC as it was sprayed seems to have a short residual effect. In spite of that it is believed that remarkable results may be obtained with two sprayings every year, because of the great knock down effect of the BHC, and the long life cycle of the insect (about 300 days)."

LEISHMANIASIS

Carrera Cobos, T. Anotaciones sobre la leishmaniosis selvática americana o cutáneo-mucosa. [**Notes on Muco-cutaneous Leishmaniasis**] *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1953, Apr., v. 1, No. 2, 76–90, 2 figs. [12 refs.]

During the past year [?1952] the author has had under his care and observation several cases of cutaneous leishmaniasis in the western Cordilleras, Suscal, Gualleturo and the neighbourhood, and the provinces of Azuay and Cañar and the adjacent province of Guayas (Ecuador), 10 cases in all. *Phlebotomus* abounds and the infection is found not only in man, but also in the domestic animals, dog, cat, horse, and in the agouti,

Gillies, M. T. **The Duration of the Gonotrophic Cycle in** *Anopheles gambiae* **and** *Anopheles funestus*, **with a Note on the Efficiency of Hand Catching.** *East African Med. J.* 1953, Apr., v. 30, No. 4, 129–35, 1 fig.

These observations were made from April to November, 1952, in an experimental hut at Tengeni, Tanganyika, a village 27 miles from the coast at Tanga and at an altitude of just over 600 feet.

Caught mosquitoes were examined each morning to ensure that they had fed the previous night; they were then caged. The cage was left in the hut overnight. Next morning the females were separated according to species into their respective oviposition cages and those in which ovarian development had not occurred were removed. The following morning the females which had laid eggs were counted. These figures are tabulated and graphed.

Taking into account the defects of observations based on caged mosquitoes it was shown that when the temperature exceeds 78°F. (25·5°C.) the gonotrophic cycle lasts for 48 hours in both *Anopheles gambiae* and *A. funestus*. Below 76·5°F. (24·75°C.) *A. funestus* has a 3-day cycle but in the majority of *A. gambiae* the cycle was still only 2 days at 74°F. (23·25°C.). No information is given on the interval elapsing between oviposition and the next blood meal but the indications are that the majority of females feed again the same night.

It may therefore be concluded that, in the coastal region, *A. gambiae* bites every 2nd night most of the year, while *A. funestus* is reduced to biting every 3rd night during the 5 or 6 cooler months. In the higher inland regions the cycle may be 2 days for *A. gambiae* for 6 to 7 months of the year and for *A. funestus* it may be 3 days all year round.

It was shown during this work that careful hand-catching missed 14 per cent. of the *A. funestus* females that were resting in the hut. *H. S. Leeson*

Halcrow, J. G. **Predacious Mosquito Larvae.** [Correspondence.] *Nature*. 1953, June 27, v. 171, 1167.

The author, from Mauritius, has observed cannibalism within the salt-water strain of *Anopheles gambiae*, but not in the fresh-water strains.

Third- and fourth-stage larvae are seen to seize other larvae and to feed on them: this seems to stimulate the neighbouring larvae and in a few seconds numerous larvae are feeding upon "the hapless victim, whose vigorous struggles are usually in vain". All that remains is the head capsule, but larvae can be seen even attempting to extract its contents with their mouth brushes. Pupae are not attacked.

This cannibalistic tendency causes much mortality in laboratory cultures: each morning breeding dishes are littered with head capsules.

The author points out that as long ago as 1910, Graham (*Bull. Ent. Res.*, 1910, v. 1, 51) stated that cannibalism was brought about in *A. gambiae*, by the addition of 3 per cent. common salt to the breeding water: but this was not confirmed by subsequent work. *H. J. O'D. Burke-Gaffney*

Colless, D. H. **Observations on the Flight Range of** *A. balabacensis* **Baisas** (= *A. leucosphyrus*, **auct.**). *Med. J. Malaya*. 1953, Mar., v. 7, No. 3, 179–84, 2 figs.

Anopheles balabacensis was formerly grouped with other species of *Anopheles* under the name *A. leucosphyrus*.

In Northern Borneo the flight of this mosquito was studied in the Timbau valley, an offshoot of the Tambunan Plain. The breeding places are at the edges of the plain among the hillsides, ravines and jungle. Spleen and parasite rates were recorded and found to be lower as the distance from the mosquito breeding places increased. A statistical analysis was made of the figures obtained from children between the ages of 2 and 13 years. The actual variates examined were, splenic enlargement in centimetres, distance from the breeding places in yards and the number of breeding places.

It is realized that there are many sources of error and some of these are discussed; however, the "effective flight range" beyond which malaria carried by *A. balabacensis* becomes negligible in this area is about half a mile. *H. S. Leeson*

Shibata, S. **Criteria of the Growth Stages of Anopheline Larvae. A Morphological Study on *Anopheles hyrcanus* var. *sinensis*.** Reprinted from *Bull. Yamaguchi Med. School.* 1953, Feb. 28, v. 1, No. 1, 37–48, 3 figs. & 3 pls.

"Two series of morphological observations, based upon the collections of larvae from different natural sources and the rearing experiments in the laboratory, have been carried out in *Anopheles hyrcanus* var. *sinensis*, in an attempt to obtain some clues for the determination of the larval instar. The results obtained can be summarized as follows:

"1. The number of ramifications [branches] of the hair No. 6 on the third abdominal segment can serve as the most reliable criterion for the determination of the larval growth stages, because the ramification shows no variations according to the different districts.

"2. The maximum transverse diameter of the head seems also useful in this respect, but because of a greater degree of variations according to the different districts its usefulness is limited to the larvae collected in the same district."

Mandoul, R. & Pestre, A. Conception actuelle de la pathologie générale des paludismes humains. [**Present Concepts of the General Pathology of Human Malaria**] *Algérie Méd.* 1952, May, v. 56, No. 5, 253–76, 3 figs. [61 refs.]

The authors discuss the early development of the malaria parasite in the host and the evolution of an attack of malaria in the light of recent work, particularly that of Shortt and Garnham. Treatment and control of malaria (both chemotherapeutic and entomological) are also considered.

[The reviewer has found it impossible to summarize this paper which should be read in the original by those interested.] *B. G. Maegraith*

Nauck, E. G. Immunitätsprobleme bei Malaria. [**The Problem of Immunity in Malaria**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1953, June, v. 4, No. 3, 285–98. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The article offers a critical synopsis on malarial immunity in man, mammals and birds. Natural resistance, acquired immunity and premunition, influence of extra- or intraerythrocytic development of parasites, cellular and humoral defence reactions and the presence of antibodies are discussed. Literature up to 1952 is reviewed."

Voss, E. A. Über angeborene Malaria. [**Congenital Malaria**] *Arch. f. Kinderheilk.* 1951, v. 143, No. 3, 113–20. [25 refs.]

The author briefly reviews the literature on " congenital " malaria (defined by Eckstein as [abstracter's translation] " the birth of a child in an environment and under conditions in which infection of the new-born by anopheline bite can be excluded "). He gives details of 2 cases which he regards as coming into this category, seen in his clinic during the winter in Kassel.

The mothers both had histories of previous malaria but had been free of attacks for some years before the present children were born. Parasites were not found in either mother. The children were both about 2 months old when malaria parasites were discovered in them. Both were anaemic and had very large spleens. One had furunculosis and an enlarged liver. This child did not respond to treatment, and died. There was apparently no autopsy. The other recovered. In the former case parasites [species not stated] were found first in the bone marrow; they were detected for the first time in the blood during treatment with atebrin [mepacrine]. In the latter, the blood contained *P. vivax* parasites. Parenteral administration of atebrin was successful.

The author considers that the intact placenta probably acts as a filter through which parasites cannot normally pass. Infection of the foetus occurs as a result of placental damage arising from rigor during a maternal malarial attack or some local accident. Intra-uterine infection leads to foetal death. Infection of newly-born living children probably occurs during birth.

[The review of the literature and the discussion are interesting. The cases quoted are not convincing.] *B. G. Maegraith*

Corcos, A. Sur un cas de tétanos post-quininique. [**A Case of Tetanus After Quinine Administration**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 283–5.

Eckhard, G. **Clinical Observation on " Resochin " in the Treatment of Malaria.** *East African Med. J.* 1953, Mar., v. 30, No. 3, 115–19.

The author reports the clinical effects of treating 49 African infants aged 6 months to 2 years suffering from *P. falciparum* malaria in Tanganyika with Resochin, the Bayer preparation of chloroquine. The drug is dispensed in 0·25 gm. tablets, and dosage was calculated, as the makers recommended, on the basis of age. Administration of the tablets was by " pushing them into the baby's throat ". Thirty-six infants had Resochin only, and 13 received this drug and various other treatments for concurrent diseases. Diagnosis was by finding parasites in blood films. Clinical improvement occurred in 24 hours in 47 cases, and parasites disappeared from the blood films by the third day. Two infants showed delayed clinical improvement, and mepacrine treatment was added in their cases. The author's opinion is that Resochin is a useful and apparently safe means of treating *P. falciparum* malaria in infants.

He gave the drug to one Asian and 3 European patients, all adults. The Europeans all complained of giddiness, nausea, and feelings of faintness. The Asian seems to have suffered from heart disease before he got an attack of malaria, and he was treated with parenteral mepacrine, and oral proguanil, to be followed by Resochin. However, he died on the fourth day of his illness with symptoms suggesting acute heart failure. The author considers that this drug should be available only with a doctor's prescription, and its use in adults should be under close medical supervision. *S. Bell*

Hale, T. R. & Halpenny, G. W. **Malaria in Korean Veterans.** *Canadian Med. Ass. J.* 1953, May, v. 68, No. 5, 444–8, 3 figs. [21 refs.]

This report deals with the occurrence of benign tertian malaria in soldiers who returned from the Canadian Brigade of the Commonwealth Division serving in Korea to the area served by a " veterans hospital " in Montreal during 1952.

Of 1,350 men, 152 developed benign tertian malaria. The attacks were of a mild type and the initial clinical picture was often quite atypical. The Korean strain of *P. vivax* has a long latent period of 8–9 months; the disease is contracted during the summer months only and the first clinical symptoms become manifest in the following spring or summer.

Seventy-five per cent. of the attacks occurred within 3 months of stopping suppressive paludrine [proguanil]. Thirty-four per cent. of the patients showed abnormalities in the Wassermann and Kahn tests, nearly all returning to normal within a few months without anti-syphilitic therapy. Fifty-five per cent. of those affected had abnormal liver function tests, the highest percentage of abnormal results being obtained with the cephalin-cholesterol flocculation test.

Of 77 patients treated with chloroquine 35 per cent. had recurrences within 3–6 months. Of 91 patients treated with chloroquine and primaquine only 1 per cent. had recurrences within 3–6 months.

Primaquine is probably the most efficient and least toxic of the existing members of the 8-amino-quinoline series. *George R. McRobert*

Jones, S. A. **Experiment to determine if a Proguanil-Resistant Strain of *P. falciparum* would respond to Large Doses of Pyrimethamine.** *Brit. Med. J.* 1953, May 2, 977.

The author, who had not had malaria before, allowed himself to be bitten on August 21st, 1952, in Kenya, by 5 *Anopheles gambiae* infected with a proguanil-resistant strain of *P. falciparum*, imported from Malaya. Parasites appeared in his peripheral blood on September 1st, and on that day 50 mgm. pyrimethamine was given, and the dose was repeated on the next day. On the third day a total of 350 mgm. was given but the number of parasites in the blood continued to increase, so that the attack of malaria was terminated by using quinine and chloroquine. This experiment showed that the proguanil-resistant parasites were also resistant to pyrimethamine. The author considers that it has been a wise policy not to subject the African population in Kenya to large-scale treatment with proguanil, since generally the East African strains of malaria parasites seem very sensitive to pyrimethamine. He hopes that soldiers from E. Africa serving in Malaya will not be allowed to return home carrying gametocytes of Malayan strains of parasites. [In a letter to the *Brit. Med. J.*, 1953, July 18, 149, E. J. Curran, Deputy Director of Army Health, Far East Land Forces, records that African troops in Malaya continue to take their regular dose of 0·1 gm. mepacrine for 4 weeks after leaving Malaya and that, in addition, those who have acquired benign or quartan malaria in Malaya receive a standard course of quinine + pamaquin or of chloroquine + primaquine.] *S. Bell*

Jaswant Singh, Ray, A. P., Basu, P. C. & Misra, B. G. **Pyrimethamine in Treatment of Vivax Malaria. Preliminary Report.** *Brit. Med. J.* 1953, June 6, 1260.

The authors record the effects on pyrexia, and parasites in the peripheral blood, of 30 patients having *P. vivax* malaria who attended hospitals in Delhi State, and who were treated with a single oral dose of 25 mgm. pyrimethamine (Daraprim). In an attempt to determine the influence of immunity the patients were grouped into those who had had malaria previously (17) and those who had not had malaria before (13).

Within 72 hours after treatment all the patients were afebrile, and, with one exception, all were free from asexual parasites in the peripheral blood. Gametocytes, however, were much slower in disappearing from the blood.

The authors regard the effectiveness of so small a dose of pyrimethamine against *P. vivax* parasites as remarkable, and consider that further work is indicated.

[While the authors suggest from their figures that clearance of symptoms and asexual parasites was more rapid in those who had a previous history of malaria, in fact the differences between the percentages for the 2 groups are not twice as great as the standard errors of those differences. No indication of the age or weight of the patients is given.] *S. Bell*

Covell, G. **Treatment of Acute Malaria.** [Correspondence.] *Brit. Med. J.* 1953, July 4, 41.

In this letter, Sir Gordon Covell, adviser on malaria to the Ministry of Health, warns of the unfortunate results which might follow the treatment of malaria in Britain through misunderstanding of the mode of action of some of the new antimalarial drugs.

For treatment of the acute attack in non-immunes, particularly in the case of *P. falciparum* malaria, a powerful immediate schizonticidal action is essential. This may be attained by the use of chloroquine, amodiaquine [camoquin], mepacrine or quinine. The schizonticidal action of proguanil and pyrimethamine [daraprim], on the other hand, is not sufficiently rapid to warrant their use, unaided, for treatment of acute attacks of malaria in non-immune subjects.

Because of the very small dose of pyrimethamine required to produce the maximum schizonticidal action, it has been hailed in an article in the lay press as "the most potent antimalarial drug the world has yet been given". In some quarters it is therefore assumed that it is the drug of choice in the treatment of acute malaria; but the fact that its action is slow and cannot be accelerated by varying the dosage is not always appreciated.

Proguanil and pyrimethamine possess qualities rendering them particularly suitable for prophylaxis of malaria, but for treatment of acute attacks in non-immune subjects they should not be used except together with some more rapidly acting schizonticide. It is suggested that to avoid any possibility of error and consequent mishaps which might follow the use of either of these two drugs as the sole treatment for acute attacks, each container might with advantage be labelled "Not to be used unaided for the treatment of acute malaria in non-immune subjects".

H. J. O'D. Burke Gaffney

Gunther, C. E. M. & Wright, W. G. **Further Observations on Proguanil in New Guinea.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1953, Mar., v. 47, No. 2, 156–8.

Gunther [this *Bulletin*, 1951, v. 48, 523] reported on the value of proguanil as a malarial prophylactic in New Guinea, but when breakthrough occurred he suggested that proguanil-resistant strains of parasites might be the explanation [Gunther *et al.*, *ibid.*, 1952, v. 49, 666]. He admits that since many of these malarial attacks were successfully treated with proguanil it is unlikely that proguanil-resistance was the explanation. In this paper the occurrence is reported of 20 cases of proved malaria and 4 cases of clinical malaria in a group of 625 white people who had been advised to taken 100 mgm. of proguanil daily. The authors consider that "regular" prophylaxis must allow for occasional lapses from daily dosage, and their standard is at least 5 daily doses in a week. During observation over 19 months they found 7 attacks of malaria among those who took proguanil regularly. Among those who took the drug irregularly, by which is meant less often than 5 doses each week, there were 13 attacks of malaria. The remaining 4 attacks occurred in persons not taking any drug prophylaxis. The authors consider that these observations do not detract from the value of proguanil as a prophylactic. *S. Bell*

Canet, J. Résistance à la paludrine au cours de la prophylaxie collective du paludisme hyperendémique à *Pl. falciparum* en Indochine. [**Proguanil Resistance During Mass Prophylaxis of Hyperendemic *P. falciparum* Malaria in Indo-China**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 2, 230–45, 4 charts. [23 refs.]

The studies here recorded were carried out in 6 villages located on a plantation near Honquan in the hyperendemic malarial zone of northern Cochin, China, where 90 per cent. of the infections are caused by *Plasmodium falciparum*. Their object was to assess the respective value of paludrine [proguanil] and nivaquine [chloroquine] in the mass prophylaxis of malaria.

The adult inhabitants of 3 villages were subjected for 18 consecutive months to a weekly régime of 0·3 gm. of proguanil given in a single dose; children received 0·2 gm. or 0·1 gm. each week, according to age. In 3 other villages the inhabitants were given chloroquine in the same dosage and for the same period. The results for the 6 villages are given in detail.

In the villages where proguanil was used, the parasite rate was at first greatly reduced and remained at a low level for several months, but began to rise from about the 7th month. Malarial attacks began to occur towards the 12th month of treatment; the numbers rose sharply a month later and by the 15th month the outbreak had reached serious proportions. Thus the clinical evidence indicated that resistance to the drug on the part of *P. falciparum* had begun to develop by the 13th month. Moreover this resistance was evidently of long duration, since in one village where treatment with chloroquine was substituted for it over a period of 7½ months, the response to proguanil remained equally unsatisfactory when distribution of the latter drug was once more resumed.

In the villages where chloroquine was given, no loss of efficacy on the part of the drug was noted; and after 40 months of uninterrupted distribution the malarial indices and morbidity figures remained stable at a satisfactory level.

The author concludes that proguanil is not suitable for prolonged mass prophylaxis in a hyperendemic area; it is effective for a limited period, not exceeding 7 or 8 months at most; beyond this it does not offer sufficient security of protection. He suggests its substitution by some other antimalarial drug after the first 6 months of treatment, or the alternation of proguanil with chloroquine prophylaxis, so as to minimize the risk of producing biguanide resistance. [For previous work by the author on related subjects, see this *Bulletin*, 1949, v. 46, 328, 521, 705; 1950, v. 47, 205, 206; 1951, v. 48, 440.] *G. Covell*

Logan, J. A. **The Sardinian Project—an Experiment in Malaria Control by Species Eradication.** Reprinted from *Proc. Inst. Civil Engineers*. 1953, Apr., Pt. 3, 11 pp.

Anopheles maculipennis labranchiae was responsible for severe malaria throughout much of Sardinia, which has 1·25 million people and is 9,226 square miles in area. Counterpart funds derived from the sale of relief goods were available on the closure of UNRRA, and an experiment in the eradication of an indigenous vector of malaria seemed a suitable form of expenditure which might be of permanent advantage rather than mere temporary ease. An organization symbolized as ERLAAS was set up and was much assisted by the Rockefeller Foundation, setting about its experiment in the following order:—

1946. Entomological survey.

1946–7 and 1947–8. Winter campaigns against adult mosquitoes, with DDT at 2·0 gm. per sq. metre.

1947. Experimental work with larvicides.

1948. Application of a DDT-oil-Triton larvicide to all water areas weekly during the summer.

1948–9. Imagocidal and larvicidal work in remaining positive areas.

1950. Check on eradication, with some additional application of larvicides.

The attempted eradication was not successful. *A. m. labranchiae* remained present in 1950, but in minute numbers. Despite general discontinuance of control only one out of every 5,000 water areas searched in that year contained larvae, and these in very small numbers only; the failure of the species, once it had been greatly reduced, to extend rapidly from its residual foci in the absence of intentional obstacle is unexplained and presents tantalizing questions, as does also the usurpation of its breeding places by *A. hispaniola*, a species not previously recorded in Sardinia. Though in one sense a failure, the expenditure of 6 billion lire (3·4 million pounds sterling) reduced the annual malaria cases from 78,173 in 1944 to 9 in 1951, caused this suppression of *A. m. labranchiae* and a break in transmission which has proved to be much more than ephemeral, and exposed the chance of invasion of evacuated breeding sites by other species, which may have much bearing on other schemes. *G. Macdonald*

Livadas, G. **Is it Necessary to Continue Indefinitely DDT Residual Spraying Programmes? Relevant Observations made in Greece.** *Riv. di Parassit.* Rome. 1953, Jan., v. 14, No. 1, 61–6. [14 refs.]

The programme of malaria control throughout Greece between 1946 and 1950 included universal imagocidal work and much use of larvicides. After 1950 routine work was stopped in two great areas, Crete and the Peloponnese, and an inspection system substituted, the principle being that

recrudescence of malaria or reappearance of numerous anophelines would be followed by local resumption of DDT application.

In Crete 856 villages had previously been treated. In neither of the years 1951 and 1952 was there any need to resume spraying.

In the Peloponnese 995 villages had been sprayed. In 1951 there were 6 fresh cases of *Plasmodium vivax* malaria in 4 villages, and anopheline recurrence in 27, which required resumption in 31 villages. In 1952, 29 cases of *P. vivax* malaria in 9 villages and anopheline recurrence in 29 demanded resumption.

After the promising findings of 1951, routine work was stopped in all but 269 of the remaining 3,215 villages of Greece, work being continued in those with the worst malarial reputation. Resumption of work was only necessary in 51. It is notable that in the area where *Anopheles sacharovi* is thought to have become resistant to DDT there has been no reappearance of malaria.

The author concludes that there has been a near-complete eradication of the malaria parasite, which has made great economy possible though the situation cannot be expected to last and vigilance is necessary.

[The author does a service in presenting data which must have an important influence on the general policy of malaria control.]

G. Macdonald

Dowling, M. A. C. **Control of Malaria in Mauritius. Eradication of *Anopheles funestus* and *Aedes aegypti*.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1953, May, v. 47, No. 3, 177–89, 2 figs. Discussion 190–98 [Macdonald, G.; Soper, F. L.; Covell, G.; Bertram, D. S.; Busvine, J.; Blair, D. M.; Dowling, M. A. C. (in reply); Fairley, N. H. (President)].

The general scope and nature of the Mauritius Malaria Eradication Scheme has been previously described [this *Bulletin*, 1950, v. 47, 321; 1951, v. 48, 327; 1952, v. 49, 367] and is here brought together as a complete story from start to termination. Briefly, the technique employed was residual spraying, originally by means (in different areas) of DDT, 1·1 to 1·6 gm. per sq. metre, or gamma BHC 0·13 to 0·21 gm. per sq. metre, every 6 and 3 months respectively. During the work BHC was abandoned and DDT used universally. There was no full preliminary survey, either parasitological or entomological, and its lack was felt towards the end of the work. Work was ended after 3 years, when a maintenance scheme was substituted; the position at this time was that clinical malaria had almost entirely disappeared; the parasite rate in children had dropped from 9·5 to 0·05 per cent., and the notifications of malaria from 105 to 0·05 per 1,000 population; the general death rate had dropped from 27·2 to 14·8 per 1,000 and the infant mortality rate from 150 to 80·8. An elaborate search for malaria cases in 1952 included the examination of over 40,000 blood films, only 47 being found positive.

Before the start of the scheme *Anopheles funestus* was very common, but it totally disappeared from the scene at the end of 1950, since when it has not been found in either adult or larval stage. *Aëdes aegypti* also totally disappeared in 1949. *A. gambiae* was prevalent though less numerous; the adult form became very rare in houses, only 3 being found in 7,292 examined in 1952, but remained common in cowsheds and breeding continued undisturbed. [It is not clear whether adult *A. gambiae* were to be found in treated cowsheds or whether some had been left untreated.]

In 1952 a review of progress showed that malaria had been reduced to an insignificant level and indicated that an attempt to eradicate *A. gambiae* might be unduly costly, for which reason the programme was ended, giving place to maintenance works. These are to include some major draining, discriminatory use of residual insecticides and of larvicides and a careful check to limit the importation of active malaria cases and detect incipient epidemics.

The author is diffident in assessing the value of the work. *A. funestus* and *Aëdes aegypti* have been eradicated, and *A. gambiae* does not now carry malaria, but the scheme is said to have been costly and similar results might have been secured by one more conservatively designed. In discussion Macdonald questioned this diffidence, pointing to the author's statement that cheap control had only been made possible by preliminary eradication of the main vector, one of only 2 species whose eradication by adult destruction had been shown possible. He thought that the reasons for the escape of *A. gambiae* deserved careful study. Soper praised the eradication of *Aëdes aegypti* and *A. funestus*; he questioned the general assumption of relative harmlessness of *A. gambiae* and regretted that the programme had not been continued in a last effort to eradicate it, possibly by means similar to those adopted in Brazil against that species. Covell pointed to the questions raised by the different susceptibility of the 2 anopheline species, and said that in a Nigerian scheme *A. funestus* had similarly been eradicated; he thought that the *A. gambiae* which do not now feed on man might well do so again when opportunity presented itself. Bertram discussed the persistence of *A. gambiae*, thinking that if there were 2 separate races, strictly anthropophilic and strictly zoophilic, eradication of the former by house spraying might be possible, though if there were one mixed race it might be impossible. He also pointed to the possible fallacy in deducing from the absence of living mosquitoes in treated houses that they did not enter; they might have done so and been killed or repelled. Busvine spoke of prevention of importation of *A. funestus* by air, and Blair asked for detailed statements of cost.

In reply Dowling said that he thought a specifically zoophilic race of *A. gambiae* existed in Mauritius; the question was being investigated. Eradication of that species would certainly be unjustifiably expensive, and it seemed probable that it was a minor vector only; it does apparently continue to enter houses though only in very small numbers. Introduction of adult mosquitoes by air is possible, and *A. squamosus* had been found on an aircraft. He also gave some details of cost. The President, Sir Neil Hamilton Fairley, congratulated the author and asked that in considering the apparent failure to eradicate *A. gambiae* one should remember the immensity of the success achieved. *G. Macdonald*

Hamid, A. **Anti-Malaria Scheme for the Lahore Corporation Area and its Working for the Period from 9th July, 1951, to 31st December, 1952.** *Pakistan J. of Health.* 1953, Apr., v. 3, No. 1, 13–24, 1 coloured map on pl. & 4 charts.

The present control programme includes a combination of larvicidal and imagocidal measures. Larvicidal work is organized on the zonal pattern with central inspectors, now usually accepted; many techniques are adopted, and the most efficient larvicide is a formulation of 0·25 per cent. Gammexane Liquid Larvicide in a mixture of diesel and furnace oils. The residual insecticides used are DDT and Gammexane P.520, each applied

at a dose of 100 mgm. per sq. ft. (1·1 gm. per sq. m.). They were generally applied in rural and suburban areas, but only in a discriminatory manner in the town itself. Two applications with a 3-month interval were made in 1951 and one in 1952.

Clinical malaria cases were fewer than in untreated villages, school attendance increased, the spleen rate dropped from 2·6 to 0·9 per cent., and anopheline densities were one-tenth of those outside the area. The mean cost per head of population was 7½ annas (8½d.) per annum.

The account is illustrated by a map, and elaborated by details of cost, climate, and normal seasonal variations in anopheline incidence.

G. Macdonald

Thompson, P. E., Moore, A. M., Reinertson, J. W. & Bayles, Anita. **Antimalarial Activity of β-Resorcylic Acid and Analogs and Reversal by *p*-Hydroxybenzoic Acid.** *Antibiotics & Chemotherapy.* New York. 1953, Apr., v. 3, No. 4, 399–408, 1 fig. [13 refs.]

In this investigation the examination of simple benzoic acid derivatives and related compounds for antimalarial activity has been carried out. A strain of *P. lophurae* was used in chicks which were infected by intravenous injection of 10^9 parasites per kgm. of weight. Drug was administered in the diet for 5 days starting on the day before infection and the effect on parasitaemia was noted in stained slides on the fourth day after infection. For comparison purposes the quinine equivalent—the ratio of MED [minimal effective dose] of quinine to that of the drug under test—was calculated. For detecting antagonism to antimalarial drugs 4 groups of birds were inoculated with *P. lophurae*, of which group 1 received no treatment; group 2 was treated with drug alone; to the diet of group 3 (which was similar to that of group 2) was added the potential antagonist; group 4 was treated with the potential antagonist alone at a level which did not affect the parasites. A substance was concluded to have an antagonistic action when the degree of parasitaemia in treated birds approximated to that of the control group 1.

In all, 101 compounds were tested and 18 of them showed suppressive activity, but for details the original paper should be consulted. From the point of view of activity and lack of toxicity β-resorcylic acid with a quinine equivalent of 0·8 was of chief interest. It acted more slowly than quinine and besides its activity against *P. lophurae* in chicks it showed activity against this parasite and *P. cathemerium* in ducks. However, it had little or no activity against *P. falciparum*. Parahydroxybenzoic acid proved an antagonist to the resorcylic acid and related compounds, and it is regarded as probable that the former substance plays some part in the metabolism of plasmodia.

J. D. Fulton

Thurston, June P. **The Action of Dyes, Antibiotics, and some Miscellaneous Compounds against** *Plasmodium berghei*. *Brit. J. Pharmacol. & Chemotherapy.* 1953, June, v. 8, No. 2, 162–5. [16 refs.]

The action of the substances named in the title on *P. berghei* has been examined by the technique previously described by the author [this *Bulletin*, 1950, v. 47, 1183]. The inoculum given to mice contained 1 million parasites, being smaller than that previously used since it appears that light infections are more susceptible to drugs than heavy infections. The drugs were given intraperitoneally once daily for 4 days, starting a few hours after inoculation. Stained blood films were examined on the fifth and seventh

days. The minimum effective dose of a drug was one which reduced parasitaemia to one-fiftieth of that in control birds. The results of the tests are recorded in a table and are compared with those in the literature for *P. gallinaceum* by using the quinine equivalent which is the ratio of the minimum effective dose of quinine over that of the drug under test. It was found that methylene blue was the most active of a series of dyes. A number of well-known antibiotics were inactive but aureomycin and terramycin showed activity. Some antimonials affected *P. berghei* but neoarsphenamine did so only in a minor degree, and the action of marfanil was also slight. Data are given in the text for a number of miscellaneous substances. *J. D. Fulton*

Thurston, June P. **The Morphology of** *Plasmodium berghei* **before and after Treatment with Drugs.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1953, May, v. 47, No. 3, 248–56, 2 figs. [26 refs.]

The author has previously reported on the morphological changes produced on trophozoites of *P. berghei* by a number of drugs [this *Bulletin*, 1951, v. 48, 869]. The changes which occur in trophozoites and gametocytes of *P. berghei* infecting mice treated by a further series of drugs, one of them the metabolite of proguanil [Carrington *et al. ibid.*, 1952, v. 49, 362], are briefly described. The changes in morphology after treatment of *P. berghei* infections with daraprim are correlated with infectivity. It was found that 12 hours after such treatment trophozoites of *P. berghei* were normally infective, and infectivity was not entirely abolished even after 48 hours. The difficulty sometimes experienced in demonstrating the pigment of *P. berghei* has been partly overcome by the use of the phase contrast microscope or by staining films with 0·5 per cent. eosin. Evidence for the disappearance of the haemoglobin of the host red cell during growth of the parasite was obtained by staining with leuco-fuchsin [this *Bulletin*, 1948, v. 45, 25]. Daraprim and some other drugs attacked early schizonts and affected nuclei, in contrast to pamaquin and methylene blue which primarily affected cytoplasm. Mepacrine and chloroquine caused clumping and extrusion of pigment and affected parasite cytoplasm before nuclei. The changes described resemble those already described for other malaria parasites.
J. D. Fulton

Rodhain, J. La spécificité biologique du *Plasmodium vinckei*, Rodhain. [**The Biological Specificity of** *Plasmodium vinckei* **Rodhain**] *Ann. Inst. Pasteur.* 1953, Apr., v. 84, No. 4, 672–83, 2 figs.

The author continues his studies on *Plasmodium vinckei* [this *Bulletin*, 1952, v. 49, 1101]. He first describes in detail the effect of the parasite on white mice, 70 of which were inoculated; 73 per cent. died of malaria usually between the 8th and 10th day after inoculation, with 80 per cent. of the erythrocytes parasitized. Reticulocytes were rarely invaded (*e.g.*, 7 or 10 per cent.), though reticulocytosis preceded cure. Haemoglobinuria occurred in 9 mice. Next he infected 9 *Thamnomys surdaster*, and 4 animals died of the infection; in the remainder the disease became chronic and parasites persisted for over 2 months. White rats, cotton rats, Syrian hamsters, *Steatomys opimus*, and African fruit bats failed to become infected with *P. vinckei* in contrast to their response to *P. berghei* which is virulent to them all. Removal of the spleen of white rats, cotton rats and hamsters sometimes allowed mild infections to take place. The most

interesting part of this study relates to cross immunity experiments with the 2 rodent parasites: mice which had recovered from 1 or 2 infections with *P. vinckei* proved completely susceptible to various strains of *P. berghei*; infections in a hamster and a fruit bat behaved in much the same way.

Transmission experiments were attempted in conjunction with Professor Wanson, with *Aëdes aegypti*, *Anopheles stephensi* and *A. maculipennis*—all with negative results; it is suggested that *P. vinckei* is strictly adapted to *A. dureni*. *P. C. C. Garnham*

TRYPANOSOMIASIS

Maillot, L. Répartition des glossines en Afrique Équatoriale Française. [**Distribution of Species of *Glossina* in French Equatorial Africa**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 2, 195–7.

The paper gives details of the geographical distribution of the 12 species of *Glossina* which occur in the territory. *P. A. Buxton*

Tanganyika. **Annual Report of the Tsetse Survey and Reclamation Department 1950** [Lloyd, H. M., Director]. 12 pp., 1 coloured folding map. 1952. Dar es Salaam: Govt. Printer. [1s.]

———— **Annual Report . . . 1951.** 16 pp., 1 coloured folding map. 1952.

These two reports can be summarized together. They contain accounts of surveys of the tsetse position in many parts of Tanganyika, the advances and retreats of the fly, successful and unsuccessful control measures, reclamation of land and the cost of each operation in man/days of labour.

Discriminative clearing and settlement of the people are important measures and such work is recorded in its own district report; these are all grouped together under the names of the 8 Provinces. The species of tsetse fly encountered and the Provinces where they occur are: *Glossina swynnertoni* in Central, Lake and Northern, and in 1950 in the Ngeza district of the Western Province, though it is thought to have died out in 1951; this point will be further investigated. *G. morsitans* in Central, Lake, Southern, Southern Highlands, Tanga and Western; in some places advances are reported. *G. pallidipes* in Lake, Northern, Southern, Southern Highlands and Tanga. *G. brevipalpis* in Lake, Southern Highlands, and Tanga and a few specimens from trains. *G. longipennis* in Northern and Tanga; in 1950 this species was recorded for the first time in the Ardai-Kissongo pilot scheme. *G. austeni* is reported from the Tanga Province only. *G. palpalis* was found in 1951 in the Mori river area of the North Mara District of Lake Province. Several cases of sleeping sickness occurred in the settlement along the valley and it was considered that it had been caused by *Trypanosoma gambiense*. Other cases of sleeping sickness were reported from other parts of the Lake Province and in the Western Province.

Two cases of sleeping sickness occurred among railway officials on the Mwanza line. It was feared that infected flies might be carried to Tabora and an investigation was started in 1950 and completed in 1951. In the

report for 1951 the dispersal of tsetse flies by trains receives special attention. The catches are summarized in 4 folding tables. The species caught on the trains was mainly *G. morsitans* but there were a few *G. brevipalpis*; it is obvious, however, that large numbers are missed. Experiments have been carried out in Kenya with Todd's Insecticidal Fog Apparatus but deflying of trains has since been discontinued there. In view of this experience it is felt that in Tanganyika deflying should be confined to the roads and if the fly density increases along the railway the position can then be reviewed. *H. S. Leeson*

Glasgow, J. P. & Wilson, F. **A Census of the Tsetse-Fly** *Glossina pallidipes* **Austen and of its Host Animals.** *J. Animal Ecology.* 1953, May, v. 22, No. 1, 47–56, 2 figs.

This work was done at Nzalagobe, Kenya (lat. 0°7′N., long. 34°E.) a peninsula projecting into Lake Victoria, parts of which are 500 feet above the lake level.

The tsetse census was calculated from marked flies, released and recaptured along specially cut footpaths. The estimate came to 1,800 *Glossina palpalis* and 17,000 *G. pallidipes*. As these figures refer to non-teneral males the total population would probably be 3 times as many and amount to 5,000 *G. palpalis* and 50,000 *G. pallidipes*.

The animal census was estimated from tracks recorded for 9 weeks (17th April to 17th June, 1950) on the same paths. The animal figures are tabulated and when summarized show that the commonest were the bush-pig (15) and the bushbuck (13). Other animals include a probable population of 8 duikers, and 1 or 2 reedbuck, waterbuck, hyena, leopard and hippopotamus. From these records it is calculated that the population of probable hosts is 43, which means that each animal supports 1,163 *G. pallidipes* and that, since each fly feeds every 4 days, each animal provides food for 291 *G. pallidipes* daily and loses 17·5 gm. (just over ½ oz.) of blood to the tsetse flies. *H. S. Leeson*

Moulanier, M. & Diouf, J. Dix années de lutte contre la maladie du sommeil sur la Petite Côte du Sénégal et la région des Niayes. [**Ten Years of an Anti-Sleeping Sickness Campaign in the Coastal Area of Senegal**] *Bull. Méd. de l'Afrique-Occidentale Française.* 1952, v. 9, No. 2, 201–38, 6 folding charts & 4 folding maps.

This is an account of sleeping sickness in the coastal zone of Senegal; brief references are made to the history of the disease in this area since the latter part of the 19th century, and to the organization of control measures. The area extends from about 100 km. north of Cape Verde to the frontier with the Gambia. North of Cape Verde the country has a series of marshy hollows (*niayes*) covered mainly with oil-palms and forming good homes for tsetse flies. South of the Cape Verde peninsula it is called the *Petite Côte*, and here also the tsetse flies breed in swamps along small rivers; at the southern end is the delta of the River Salum with numerous small islands. Along the frontier with the Gambia the country gradually changes from the humid western end at the sea-coast to the much drier part inland; tsetse flies and sleeping sickness are present along this border.

Reports on sleeping sickness were published during the early years of this century but no well-organized control measures were taken until, following work by Jamot's mobile teams in 1935 and 1939, the General

Autonomous Sleeping Sickness Service was formed and began work here in 1940; the work was continued by the Mobile Hygiene and Prophylaxis Service [see this *Bulletin*, 1950, v. 47, 444].

The authors give short accounts of the course of the disease in the various parts of the area, with tabulated figures showing the numbers of new cases found every year in each of about 200 villages from 1935 (or later) to 1951. Control measures included agronomic prophylaxis [not described], medical treatment, and, in some places, prophylaxis with pentamidine which was found very effective. The total number of new cases decreased from 565 in 1949 to 105 in 1951, the corresponding indices of new infection being 1·46 and 0·06. If this rate of improvement continues, the authors think that sleeping sickness will soon disappear from the *Petite Côte* and the region of the *niayes*. Close co-operation with the Government of the Gambia is expected. *J. F. Corson*

Bose, A. N. & Bose, S. **Studies on Arsenoxide Derivatives. Part II. Pharmacology of Amidino-Arsenoxides.** *Indian J. Med. Res.* 1952, Oct., v. 40, No. 4, 517–28. [11 refs.]

Cole, B. A., Frick, L. P., Hodges, Elizabeth P. & Duxbury, R. E. **The Use of 5-Nitro-2-Furaldehyde-2 (2-Hydroxyethyl) Semicarbazone (Furadroxyl) in the Treatment of Experimental Trypanosomiasis in Laboratory Animals.** *Antibiotics & Chemotherapy.* New York. 1953, Apr., v. 3, No. 4, 429–33, 3 figs.

The substance named in the title has been tested *in vivo* against *T. cruzi*, *T. equiperdum*, *T. gambiense* and *T. rhodesiense* in mice weighing 20 to 25 gm. and in rats weighing 125 to 150 gm., after an inoculum of 100,000 organisms intraperitoneally. A 1 per cent. solution of the drug in polyethylene glycol was used for oral treatment in single or divided doses starting at the time of infection and also after 24 or 48 hours. The course of infection was followed by examination of fresh smears of tail-blood in control and experimental animals. An estimation of drug activity was based on its effect on parasitaemia and on mortality rate. The drug was found to be ineffective against *T. cruzi* but high survival rates were obtained in the other infections over a range of 75 to 200 mgm. drug per kgm. In rats it appeared to be more effective than in mice and early treatment gave the best results. Because of the low therapeutic index in mice the authors do not recommend the use of the drug in human infections. *J. D. Fulton*

Tobie, Eleanor J. & von Brand, T. **The Development of Arsenic Resistance in *Trypanosoma gambiense* and its Influence on Parasitaemia.** *J. Infect. Dis.* 1953, Mar.–Apr., v. 92, No. 2, 132–8, 1 fig.

This investigation deals with the preparation of a strain of *T. gambiense* resistant to reduced tryparsamide and a study of the resultant changes in the character of the infection in white rats, white mice, and guineapigs when marked resistance to the arsenical had been attained. The strain had been maintained in mice since 1934 after isolation from a patient in London in 1921. Rats were found by the authors to be the most suitable hosts in which to propagate the strain. Resistance was produced by the method of Yorke *et al.* [this *Bulletin*, 1932, v. 29, 293]. When the strain showed a 600-fold resistance to the drug it was maintained in rats without alteration of resistance for some months and a study of the character of infection was

Dasyprocta variegata, and opossum, *Didelphys paraguayensis*, and other sylvatic rodents. The paper consists of general remarks on the infection and the author illustrates them by details of a man of 20 years from Cañar, with several typical ulcers on the right arm which began 5 months before as an itching but painful papule, with irregular fever, and which later ulcerated with serous and blood-tinged discharge. Leishmaniae were seen in the discharge. Cure was obtained from administration of antimonials. Up to the present, no patient has shown the necrotizing oro-nasal lesions. *H. Harold Scott*

FEVERS OF THE TYPHUS GROUP

Djourichitch, M. Quelques caractéristiques de la grande épidémie de typhus survenue, au cours du printemps et de l'été 1942, chez les réfugiés sur les bords de la Drina en Yougoslavie. [**Features of the Large Epidemic of Typhus Occurring in Spring and Summer 1942 in Refugees on the Banks of the Drina River, Yugoslavia**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 286–7.

Epidemic typhus has been known in the countries which now constitute Yugoslavia since before the first World War. Conditions there were primitive and sanitation was bad. During the first War, a large epidemic attacked troops and later civilians in Serbia and the mortality was 70 per cent.

During the second World War, nearly 20,000 refugees were established on the right bank of the river Drina in the spring of 1942. They came from areas where typhus was endemic, and as conditions favourable to spread of the disease were prominent (cold, poor housing, bad hygiene, widespread infestation with lice), a large epidemic broke out which attacked almost all the refugees. In 2 or 3 months, there were more than 10,000 cases in an area of 30 km. × 5 km. The striking feature was the low mortality in view of the bad conditions and hunger: it was no more than 4 per cent. in several thousand cases seen by the author.

The very old and the very young were attacked, but in small numbers and less severely than were those of adult ages.

In hospital patients with the disease, 14 per cent. of Weil-Felix reactions were negative, yet there were 24 per cent. of positive reactions in apparently healthy children of 2 to 10 years.

The author contrasts the conditions in Yugoslavia in the two Wars: in the first the epidemic attacked healthy men and was severe, with a high mortality; in the second, it attacked refugees in a very bad physiological state, the mortality was very low and the disease was mild in infants and old people. *H. J. O'D. Burke-Gaffney*

Strandtmann, R. W. & Eben, Dorothy J. **A Survey of Typhus in Rats and Rat Ectoparasites in Galveston, Texas.** *Texas Reports on Biol. & Med.* 1953, v. 11, No. 1, 144–51.

A survey of rats and their ectoparasites was carried out in Galveston, Texas, between September, 1945, and August, 1947. The only rats found were *Rattus norvegicus*. The complement-fixation test for murine typhus

was positive in 63 per cent. of 141 rats in 1945; in 58·8 per cent. of 131 rats in 1946, and in 32·7 per cent. of 110 rats in 1947. The reduction in 1947 was attributed to intensive dusting with DDT from the middle of 1946.

By far the commonest rat flea was *Xenopsylla cheopis*; among 74 " small lots " of this, 19 were found positive in animal inoculation tests for *Rickettsia mooseri*. It was uniformly present throughout each year. The index fell from 7·4 and 6·4 in the first 2 years to 1·13 in 1947. *Leptopsylla segnis* was far less abundant, and like the other fleas it showed an abrupt decline in numbers in 1947. Among 16 lots tested, 2 were found infected. *Echidnophaga gallinacea* was never very abundant; among 15 lots tested 1 was found infected. The dog flea and cat flea, *Ctenocephalides canis* and *C. felis*, were never abundant; no infection was found in the two lots tested.

The most common mite was *Laelaps nuttalli* which occurred in about 80 per cent. of the rats at the average rate of about 30 for each rat. No infection was found among 29 lots that were tested. Another mite, *Bdellonyssus bacoti* was found on about 40 per cent. of the rats, at an average rate of 2 per rat. No infection was found in any of the 19 lots tested. It was found sometimes in dwellings and was troublesome because of biting readily and causing irritation. It has been reported by some observers as capable of harbouring infection [this *Bulletin*, 1947, v. 44, 574] but the authors failed to obtain transmission from rat to rat by biting, with colonies of this and of *L. nuttalli*. They also failed to infect rats by inoculation with colonies of these mites which had fed for 2 weeks on infected rats. Larval Trombiculidae, *Eutrombicula masoni*, were found fairly often in the ears of rats. The mite *Laelaps echidninus* was almost completely absent though it was known to have been common in the area in 1933–34, and in other places in Texas at the time of the survey.

The louse *Polyplax spinulosa* was abundant, the infestation rate was about 75 per cent., and on one old rat 4,973 were found. Among 17 lots inoculated none was found infected.

No material reduction occurred among the mites or lice in 1947 when there was a striking reduction in the number of fleas and also in the number of cases of human murine typhus.

[The authors, like many other workers in the U.S.A., use the name typhus as a synonym of murine typhus or flea-borne typhus; in other countries this name, used alone, stands for historic, louse-borne typhus or, in Germany, for example, for typhoid fever.] *John W. D. Megaw*

See also p. 983, Wharton and Fuller, **A Manual of the Chiggers. The Biology, Classification, Distribution, and Importance to Man of the Larvae of the Family Trombiculidae (Acarina).**

Noad, K. B. & Haymaker, W. **The Neurological Features of Tsutsugamushi Fever, with special reference to Deafness.** *Brain*. 1953, Mar., v. 76, Pt. 1, 113–31, 6 figs. [19 refs.]

The after-effects of scrub typhus on the nervous system are not likely to be a serious problem in future years, at any rate among patients who are treated with the new antibiotics.

The authors have studied the records of 180 Australian soldiers who had suffered from the disease in New Guinea during the last war. Among these there were 106 who had been accepted as suffering from a pensionable disability or had claimed to have had a disability; 60 of them had at some

time suffered from such disorders as the neurocirculatory syndrome and anxiety states but at the time of writing only 40 still complained of symptoms referable to these conditions.

In the records of the 180 patients reference was found to the occurrence of polyneuritis in 10 cases, and in some of these numbness of various areas of the body was still complained of. Epileptiform attacks occurred at intervals in 3 patients. There were 5 cases of important psychogenic after-effects of various types; these were dementia and epilepsy, defective memory and depression, giddiness and irritability, post-infective paranoia, followed by complete recovery, and a " psychopathic " condition which still existed till the death of the patient from perforated gastric ulcer in 1948. Presumably the average severity of the 180 cases was great; but no mention is made of the fatality rates of the outbreaks during which the patients were attacked.

A special study was made of deafness resulting from scrub typhus. Although so many patients are deaf during the attacks only 9 of the 180 patients were still disabled by the condition 6–8 years later, and only 2 of these were severely affected.

A detailed and illustrated description is given of the microscopic changes found in the brain and cranial nerves of 16 men who died during the illness. Oedema and damage to the axis cylinders of the cranial nerves were the chief features and these were associated with perivascular collections of mononuclear cells. Compression of the acoustic nerves resulting from perivasculitis appears to be the cause of deafness in scrub typhus.

John W. D. Megaw

Piontkovskaya, S. P. [**The Ticks** *Hyalomma marginatum marginatum* **Koch as Carriers of Rickettsiae.** *Zool. Zh.* Moscow. 1949, v. 28, Pt. 5, 419–20, 1 pl. [In Russian.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1953, Apr., v. 41, Pt. 4, 51.]

Successive generations of *Hyalomma marginatum marginatum* Koch were reared from some of the ticks in which rickettsiae had been found in the Crimea. Examination of smears of the digestive and sexual organs of seven of the reared males and 38 of the females revealed the presence of polymorphic rickettsiae in the salivary glands, stomach, Malpighian tubes or ovaries of seven of the females. These females belonged to the second and third laboratory generations and comprised descendants of three of the original batches from the steppe zone and one of those from the mountain-forest zone.

Giroud, P., Gaillard, J. & Roger, F. La démonstration des mutants dans les rickettsioses et plus particulièrement pour l'agent étiologique de la fièvre boutonneuse, *Rickettsia conori*. [**Demonstration of Mutants in the Agents of Rickettsial Diseases, with Special Reference to** *Rickettsia conori* **of Boutonneuse Fever**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 2, 173–5.

Four strains of *Rickettsia conori* from different sources were studied by mouse-lung and yolk-sac cultivation. When adapted to the mouse lung the rickettsiae were much more slender, grew more abundantly, were less intensely stained, and ceased to grow inside the cell nuclei. Rabbits inoculated with the modified strains developed homologous antibodies and also

antibodies which immunized against proved strains of *Rickettsia mooseri*. The strains of *R. conori* when grown in yolk sacs remained characteristically of the boutonneuse type and did not give rise to antibodies of the murine type. *John W. D. Megaw*

Bell, E. J. & Pickens, E. G. **A Toxic Substance associated with the Rickettsias of the Spotted Fever Group.** *J. Immunology.* 1953, May, v. 70, No. 5, 461–72, 1 fig. [29 refs.]

The authors describe a study of a toxic substance which was demonstrated in yolk-sac cultures of 10 strains of the " spotted fever rickettsia ". Six of the strains were of *Rickettsia rickettsi* from North America, the others were of the agents of Brazilian tick-borne typhus, boutonneuse fever, South African tick bite fever, and Indian tick typhus. Attempts to demonstrate the toxins in *Rickettsia akari* and the rickettsia of North Queensland tick typhus were unsuccessful.

The highest concentration of the toxins was obtained by continuing to incubate the yolk-sac cultures for 36–48 hours after the death of the embryo chick, by introducing large doses of the rickettsiae into the yolk sacs, and by selecting yolk sacs that survived longest after inoculation.

The toxins were titrated by finding their lethal effect on mice. By the mouse neutralization test it was found that the toxin of *R. rickettsi* was neutralized by sera of patients or animals convalescent from Rocky Mountain spotted fever and also by sera of persons vaccinated by *R. rickettsi* but not by sera of persons or animals immune to Q fever, epidemic typhus or murine typhus. By the mouse test it was possible to differentiate between *Rickettsia conori* and *R. rickettsi*. The possibility of practical application of the toxin in differentiating strains of rickettsiae and in diagnosis is discussed. *John W. D. Megaw*

Aikawa, J. K. & Harrell, G. T., with the technical assistance of W. Brooks. **Effect of Cortisone Acetate on Experimental Rocky Mountain Spotted Fever in the Guinea Pig.** *Proc. Soc. Exper. Biol. & Med.* 1953, Apr., v. 82, No. 4, 698–701.

Among 25 guineapigs inoculated with *Rickettsia rickettsi* and given 1·0 mgm. of cortisone daily from the day of inoculation there were 14 deaths, compared with 18 deaths among 26 control animals not treated with cortisone. Excluding 3 mild and 8 very severe cases from each group there were 6 deaths among the 14 " moderate " treated cases and 11 deaths among the 15 moderate control cases.

In another experiment 20 inoculated animals received 5 intramuscular doses of cortisone daily—5·0 mgm. in each dose—starting on the 4th day after inoculation and continuing for 5 days. There were 16 deaths; this was the same number as in a control group of 20 inoculated animals not treated with cortisone, but the treated animals remained much livelier than the controls for 2 days after the treatment was started, and only 6 of them died during the period of treatment whereas 14 deaths occurred among the untreated animals during the corresponding period.

It was concluded that the beneficial effects of cortisone acetate were transitory. *John W. D. Megaw*

Terhaag, L. Zur Epidemiologie des Q-Fiebers. Q-Fieber in der Eifel. [**The Epidemiology of Q Fever. Q Fever in the Eifel Region**] *Arch. f. Hyg. u. Bakt.* 1953, v. 137, No. 4, 247–69, 3 figs. (1 folding). [91 refs.]

The author describes, and discusses at considerable length, the epidemiological features of an outbreak of Q fever which occurred in the spring of 1950 in the Eifel region of western Germany.

The most likely source of infection was a flock of sheep which traversed the area in the course of their migration to summer grazing grounds in the Eifel Mountains. Infection was believed to have been conveyed by airborne dust contaminated by the dried discharges from the sheep. Placental and other material discharged from the ewes at the time of lambing appeared to play an important part; there was a close association between the lambing season and the occurrence of the disease in each locality, allowing for the incubation period.

Reasons are given for believing that most of the outbreaks reported from other parts of Germany have also been associated with the migration of sheep. The author recommends that medical and veterinary practitioners should collaborate in working out a scheme for the compulsory notification of the disease in man and animals with a view to introducing legislation prohibiting the movement of flocks found to be infected. It seems likely that there would be fierce opposition to this measure from the people whose livelihood depends on the yearly migrations of their animals to and from the grazing grounds in the uplands. The discovery of an effective preventive vaccine for the animals would appear to offer a better prospect of a practicable solution of the problem.

The bibliography consisting of 91 references is a valuable feature of the paper.

John W. D. Megaw

Clavero, G., Perez Gallardo, F. & Valle, E. Cuatro casos de fiebre "Q" contraídos en el laboratorio. [**Four Cases of Laboratory Infection with Q Fever**] *Rev. Sanidad e Hig. Pública.* Madrid. 1952, Mar.–Apr., v. 26, Nos. 3/4, 199–201.

Four persons engaged in work in a laboratory where investigation into Q fever was conducted were attacked in the months of January, April, November and December, 1950. The clinical features were consistent with infection with Q fever and the diagnosis was confirmed by a rising-titre complement-fixation reaction, though attempts to recover the rickettsia by guineapig inoculation with blood taken at the height of the fever were unsuccessful. In all the cases convalescence was very slow. The source of infection was thought to have been different in each case, but it is stated that inhalation of droplets or dust produced in connexion with yolk-sac cultivation might have been responsible in every case.

John W. D. Megaw

Weyer, F. Die Beziehungen des Q-Fieber-Erregers (*Rickettsia burneti*) zu Arthropoden. [**The Significance of *Rickettsia burneti* in Arthropods**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1953, June, v. 4, No. 3, 344–82, 15 figs. [Numerous refs.]

This is a monograph rather than a paper; it deals in a comprehensive manner with the difficult problem of the part played by arthropods in the transmission of *Rickettsia burneti* among the animal reservoirs of Q fever.

Most of the author's own experimental work on the subject, as described in the paper, has already been published in papers of which abstracts have appeared in this *Bulletin*. There is also a critical review of the literature with a bibliography of about 70 references, each of which contains the full title of the article referred to.

At the time of writing the author had not seen the paper by Derrick on the epidemiology of Q fever [this *Bulletin*, 1953, v. 50, 616], but a footnote refers to this as an important contribution which is complementary to the present article.

A comment is made on the proposal, already widely adopted, to change the name *Rickettsia burneti* to *Coxiella burnetii*. The author's view is that although the organism has certain special characteristics the time is not ripe for a systematic review of the rickettsiae and that the original name does not give rise to misunderstanding. This opinion of one of the leading experts on the subject deserves consideration, but the new name has already been so widely accepted that opponents of the change are likely to find themselves in a minority.

The general impression conveyed by the paper is that little is definitely known of the part played by arthropods in the natural transmission of the infection, in spite of the large amount of experimental work that has been done on the subject. *R. burneti* has been found capable of survival and multiplication in many arthropods after artificial inoculation, but natural infection has been found only among ticks of 18 species, belonging to 8 genera; a list of the reports of recovery of the organism from ticks in every continent of the world is given in the paper. In laboratory conditions *R. burneti* multiplies so readily in human lice and bed-bugs that these fall under suspicion of being natural vectors.

[This paper and the one by Derrick, mentioned above, will be found exceedingly helpful to workers on the epidemiology of Q fever.]

John W. D. Megaw

Perez Gallardo, F., Clavero, G. & Hernandez, S. Investigaciones sobre la epidemiología de la fiebre " Q " en España. Los conejos de monte y los lirones como reservorios de la " Coxiella burneti ". [**Epidemiological Studies of Q Fever in Spain. Mountain Rabbits and Dormice as Reservoirs of Infection of** *Coxiella* (*Rickettsia*) *burneti*] *Rev. Sanidad e Hig. Pública*. Madrid. 1952, Jan.–Feb., v. 26, Nos. 1/2, 81–7.

Among 96 mountain rabbits caught in the mountains of the Province of Madrid evidence of widespread infection with Q fever was found. Of 205 guineapigs inoculated intraperitoneally with spleen suspensions of the rabbits, 103 died of a febrile infection lasting 3–4 days. No evidence of bacterial infection could be detected and in complement-fixation tests of the sera of 50 of the inoculated guineapigs, positive reactions for Q fever occurred in 29 cases at titres of 1 in 5 to 1 in 160. With the same test, sera of 54 out of 81 of the rabbits were positive. Attempts to cultivate *Rickettsia burneti* from the spleens of 14 rabbits in yolk sacs were successful in 3 cases.

Similar findings are described in a study of 229 dormice captured in the Province of Madrid.

John W. D. Megaw

Maurin, J. Déviation du complément et épreuve allergique dans la fièvre Q. [**Complement-Fixation and Allergic Tests in Q Fever**] *Ann. Inst. Pasteur.* 1953, Mar., v. 84, No. 3, 650–53.

Experiments are described which show that the complement-fixation reaction for Q fever becomes positive in healthy animals after the injection of antigens of *Rickettsia burneti* in carrying out the allergic tests for the disease. The complement-fixation test is, therefore, of no value in cases in which the supersensitivity test has previously been performed.

Two lambs of 2 to 3 months received 0·2 ml. each of Lederle Q fever antigen by subcutaneous injection into one lower eyelid, and the same amount of Q fever antigen from the Rocky Mountain Laboratory, Montana, was injected into the other lower eyelid; 24 days later 0·2 ml. of the Montana antigen was injected intradermally into each lamb. The fixation reaction, which had been negative, became fully positive (++++) 17 days after the first injections, at a titre of 1 in 16 in one lamb and of 1 in 8 in the other. The titre in both lambs rose later to 1 in 32.

Two other lambs aged one month received single intradermal injections of the Montana antigen and the fixation titre rose slowly, reaching 1 in 16 in about 2 months. *John W. D. Megaw*

Siegert, R., Peter, H., Simrock, W. & Schweinsberg, H. Versuche zur aktiven Immunisierung gegen Q-Fieber. [**Experiments in Active Immunization against Q Fever**] *Arb. a. d. Paul-Ehrlich-Inst. u.s.w. Frankfurt/M.* 1951, No. 49, 162–71, 4 figs.

In a large series of experiments tests were made of the immunizing value of large doses of Q fever vaccine prepared from yolk-sac cultures which were killed by exposure to ultra-violet rays after being purified with ether. Sera of guineapigs inoculated with various strengths of the vaccine gave positive reactions with rickettsia-agglutination and complement-fixation tests at titres whose height was related to the size and number of the doses. The average titre of the agglutination reaction on the 38th day after the first injection with the largest dose was about 1 in 6 after a single dose and about 1 in 20 after either 2 or 3 doses; for the fixation reaction the titres were about 1 in 120, 1 in 300 and 1 in 200 after 1, 2 and 3 doses respectively. The inoculated guineapigs, however, showed no worth-while immunity against infection, and the authors strongly suspect that other workers who have reported the production of complete immunity in guineapigs after inoculation with killed rickettsiae may have been using incompletely killed vaccines which caused inapparent attacks of the disease.

[Abstracts of articles by earlier workers on Q fever vaccines will be found in this *Bulletin*, 1941, v. 38, 690 (Bengtson); 1948, v. 45, 424 (Smadel *et al.*); 1950, v. 47, 1192 (Meiklejohn *et al.*); and 1951, v. 48, 30 (Payzin).] *John W. D. Megaw*

YELLOW FEVER

García Solórzano, E. Fiebre amarilla en Ecuador. [**Yellow Fever in Ecuador**] *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1953, Apr., v. 1, No. 2, 69–75, 2 maps. [14 refs.]

The last recorded case of urban yellow fever in the littoral of Ecuador occurred in Guayaquil in May, 1919. One case, sylvatic in origin, was

reported as the result of examination of a section of liver sent from Calceta, Bogotá, in September, 1951. But, says the author, if the patient had been born and had grown up in Guayaquil the death might have been attributed to carbon tetrachloride given as an anthelmintic, "as the lesion is very similar to those of yellow fever".

In 1948 an enquiry into the infestation of dwellings in different localities by *Aëdes aegypti* was undertaken and the mosquito was found in every one. DDT was used, in powder form, over collections of water and in 5 per cent. solution or suspension as a spray [presumably in buildings] around the breeding places. By 1951, of 1,325 localities 11 only were positive for this mosquito and in December, 1952, search in 380 localities discovered none positive. [These are figures given in the text. Two tables subjoined to the paper show considerable differences. In the first the figures do not seem (to the abstracter) reconcilable. There are several discrepancies and wrong additions and the totals are consequently wrong; nevertheless these totals are taken as correct in the second table and the details made out to correspond.] *H. Harold Scott*

García, E. Progresos en la lucha contra la fiebre amarilla en El Ecuador. [**Yellow Fever Control in Ecuador**] *Bol. Oficina Sanitaria Panamericana.* 1953, Mar., v. 34, No. 3, 221–4. English summary.

The *Aëdes* eradication programme in Ecuador is based on the application of DDT wettable powder to water collections, in sufficient quantity to produce a final concentration of 5 parts per million of the insecticide, combined with the discriminatory application of residual insecticides. For this latter purpose solutions or suspensions of DDT are applied to external and internal walls in the neighbourhood of occult breeding places, or those in which pupae are discovered. In 1948 *Aëdes* was found in 71 per cent. of the localities surveyed, in 1951 after this treatment in only 0·8 per cent., and in the first 3 months of 1952 all the 168 localities searched were negative.

During 1951 there were 14 viscerotomies; 8 of the specimens were positive and 1 undiagnosed, being decomposed. In the same year 20,142 vaccinations were given against yellow fever. *G. Macdonald*

Bevier, G., Torres-Muñoz, N. & Doria-Medina, J. **Yellow Fever in Bolivia, its History and Epidemiology.** *Amer. J. Trop. Med. & Hyg.* 1953, May, v. 2, No. 3, 464–82, 4 maps.

For the first time the history of the disease in Bolivia is brought together, covering the period 1867 to 1951. Though it is presented as history some of the most important happenings recorded are very recent and their description enlarges our knowledge of epidemiology.

Aëdes aegypti was probably a recent entrant to the country and had a limited distribution, which is mapped. A yellow fever epidemic probably occurred in 1867; there were certainly several in 1887 and minor ones from that date to 1932. In that year a severe outbreak involving 5,000 cases in Santa Cruz stimulated the formation of a Yellow Fever Service and the progressive elimination of *Aëdes aegypti*. This was complete in 1943 though there were 4 local re-introductions, each followed by elimination, before 1948. During this time there had been one major outbreak of *Aëdes* yellow fever, of 100 cases, and of interest because it was traced to its jungle source, and a number of outbreaks of the jungle form. These latter

occurred in known endemic areas, which are only a small proportion of the country, and their scale was sometimes notable, the bigger outbreaks affecting such numbers of people as 231, 180, 502, 159, 411, 112 and 200. Transmission was by *Haemagogus* mosquitoes normally living in the forest canopy and the epidemiology was of the normal type seen in the jungle disease.

In 1949 and 1950 an entirely new picture developed; widely distributed cases occurred more or less simultaneously, and many of them in areas previously free. Doubtless an epizootic preceded their appearance but it had not been observed. After an unusually wet season *Haemagogus* mosquitoes "left their usual habitat in the forest canopy to become house pests" and in some places "became a major pest, entering houses and biting avidly". Their larvae were not infrequently found in domestic receptacles, particularly barrels, and inspectors had difficulty in distinguishing them from those of *Aëdes aegypti*. The epidemic had the character usually associated with transmission by this latter insect; in one Province there were 1,314 known cases and 376 deaths. The total of known cases in 1950 was 1,773 but this is probably much less than the actual number.

Much of this happened in areas very difficult of access, and control has been largely through the mechanism of diagnosis by viscerotomy and vaccination. The nature of the terrain made difficulties in the path of both and termination of the epidemic was perhaps natural. It has been followed by the usual lull during which the vaccination programme is being extended.

[This paper should be seen in the original by all concerned in the epidemiology of yellow fever as the facts reported in it show that the distinction between the epidemiology of *Aëdes* yellow fever and that of the jungle type can be completely blurred.] *G. Macdonald*

Neghme, A., Albi, H. & Gutiérrez, J. Campaña de erradicación del *Aedes aegypti* en Chile. [*Aëdes aegypti* **Eradication Campaign in Chile**] *Bol. Oficina Sanitaria Panamericana.* 1953, Mar., v. 34, No. 3, 205–20, 3 figs. English summary.

Aëdes aegypti is present in the villages and towns of Chile from its northern limit to latitude 29°S., and a scheme for its eradication was required by an International Convention to which the Government subscribed. Original work on routine lines was unpromising, and for it there was substituted the principle of instillation of DDT into the water supplies entering the villages rather than the treatment of individual breeding places. The infested region is desert and all water is derived from canals coming from the mountains and emptying into village tanks, into which DDT wettable powder was inserted in such a way as to ensure a concentration of 1 part per million for 3 days, and repeated periodically. As these tanks are the source of all casual water it was thought that the insecticide would thereby reach most breeding places.

There was marked success in country districts, and in the 3 infested Provinces the *Aëdes* index was reduced between 1949 and 1952 in the following manner:—from 15 to 0·06 per cent.; from 12 to 0·04 per cent., and from 3 per cent. to zero. There was little success, however, in the town of Tocopilla, an old focus of yellow fever, despite several variations of technique; perhaps its large size favoured irregularities of water distribution and creation of hidden "mother foci" in such places as deserted houses.

An imagocidal campaign was substituted, BHC being applied at a mean rate of 0·094 gm. per sq. metre of the gamma isomer to all buildings in the infested zone, 2 applications being made with a 3-month interval. The *Aëdes* index, which had vacillated between 40 and 1·25 per cent. under the previous treatment, and was 20 per cent. when this work started, rapidly declined to zero. The cost per head of the population was 2·45 pesos.

It is concluded that DDT application to central water supplies has eradicated *Aëdes aegypti* from most of the country [the evidence of full eradication is not complete, however], but is less effective than imagocidal work in areas where hidden breeding places may remain for long times.

G. Macdonald

Kouwenaar, W. **The Reaction to Yellow Fever Vaccine (17D), particularly in Allergic Individuals.** *Documenta Med. Geograph. et Trop.* Amsterdam. 1953, Mar., v. 5, No. 1, 75–84. [39 refs.]

Ill-effects following the inoculation of yellow fever vaccine might be attributable to (*a*) multiplication of living virus, either the one intentionally given or a contaminant; (*b*) general non-specific reaction to foreign protein; or (*c*) specific allergic reaction. It is also possible that the vaccine might sensitize the individual to protein and produce a later allergic condition. Review of the literature demonstrates that these have all occurred.

A total of 1,130 persons receiving aqueous-base 17D vaccine were classified according to previous history of allergy and of previous yellow fever inoculation; they were studied by intradermal testing of the allergic, by immediate observation, and later enquiry by means of a questionary sent to all. Mild febrile reactions attributable to virus multiplication were seen after the fifth day in 7·6 per cent.; the occurrence of serum jaundice seemed unlikely, though investigation was hampered by the departure of many to places where epidemic hepatitis was common. General non-specific reactions were seen in 7·8 per cent. and were mild, while localized minor reactions occurred in about a third of the people studied. Acute allergic shock was not seen, but may have been avoided by giving progressively increasing intracutaneous doses to persons with a history of allergy. In 4 persons there was a recrudescence of a pre-existing allergy, asthma, hay fever or eczema. Early urticaria was seen in 2 allergic persons and late reactions resembling serum sickness in 9, both being commonest in those with a history of allergy. Two persons were perhaps sensitized, one to subsequent doses of vaccine and one to eggs.

The author concludes that the risk of allergic reaction is quite notable and that it will only be overcome when the scarification technique is substituted for subcutaneous injection.

G. Macdonald

RABIES

Veratti, E. **Adelchi Negri his Life and Scientific Activity.** *Scientia Med. Italica.* 1951–52, v. 2, Nos. 3/4, 662–79.

Ceccaldi, J., Saint-Etienne, J. & Audebaud, G. Nouveau cas de rage observé à Brazzaville chez une fillette de 5 ans. [**A New Case of Rabies in Brazzaville in a Child of Five**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 291–5.

Boiron, H. & Camain, R. Quelques considérations sur un cas de rage humaine observé à Dakar. [**Observations on a Human Case of Rabies at Dakar**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 2, 176–80.

This paper describes a case of rabies in an African child. Anti-rabic treatment was started. Death occurred without any symptoms of rabies being observed. At post mortem there was severe congestion of the brain but no Negri bodies on section.

Inoculation of brain material intracerebrally into mice and a rabbit produced typical symptoms and Negri bodies were demonstrated in sections.

J. Carmichael

Ordman, D. **The Occurrence and Control of Rabies in South Africa.** *Pub. Health.* Johannesburg. 1953, June, v. 17, No. 6, 383–6, 398.

The author, from the South African Institute for Medical Research, opens this paper with a brief general account of rabies in animals and man. He then points out that rabies has been known in South Africa for over 100 years, but after a long period of quiescence, it became prominent again some 60 years ago, having apparently been introduced into the Port Elizabeth area through an imported dog.

In South Africa, rabies occurs chiefly in small wild carnivores of the meercat or mongoose family (Viverridae) and also in wild cats (Felidae) which may infect domestic animals and man by biting. The dog is not a usual transmitter in the Union. The important animals are the yellow mongoose (*Cynictis penicillata*) and, to a lesser extent, the genet cat (*Genetta felina*).

From 1916–1953, 69 cases of human rabies were recorded in the Union of South Africa, 29 from bites of the yellow mongoose, 7 from the genet cat and 4 from wild cats. Rabid dogs accounted for 13 cases, and domestic cats for 9. During the same period, the disease was reported in 201 head of cattle, 124 dogs and 36 cats.

The disease is widely distributed in the Union, and occurs mainly in the Orange Free State, the Western Transvaal and Northern Cape. The distribution seems to be related to the regional density of the mongoose. The genet cat is found chiefly in the Eastern part of the Cape Province, the coast of Natal, the Transvaal lowveld and also in Zululand and Bechuanaland.

The yellow mongoose lives in small colonies in burrows and the genet cat in bush or " koppies " and sometimes in old burrows. The difficulty of controlling the disease in such wild animals is emphasized.

Towards the end of 1950, cases of rabies were recognized in the Northern Transvaal and it was soon apparent that canine rabies was being introduced into the Union from S. Rhodesia and Bechuanaland, where it is endemic. Most of the dogs infected with meercat strains of the virus in the Union showed clinical signs of " dumb " rabies, while in the other territories named and in South-West Africa the " furious " variety occurs. It seems that the local strain has become gradually adapted to the mongoose, and dogs are no longer naturally infected by it, though they can readily be infected with it experimentally.

A recent fatal case in a healthy young European emphasizes tragically the danger of veldt animals. The bite of a meercat healed and the incident was forgotten. It is pointed out that because of the long incubation period of rabies, it is easy to forget the existence of a previous bite until it is too late. Thus the number of deaths is probably underestimated. In bush districts, the disease often may not be diagnosed or even suspected. The

incubation period in South Africa is said to be 3–8 weeks after the bite of a mongoose or genet cat.

Vigorous measures against veldt animals are carried out by the Union Department of Health, and animals likely to be associated with the potential vectors are also hunted out.

The author describes the procedure for obtaining and dealing with specimens for diagnosis, the nature, use and effect of rabies vaccines, and the recent introduction of anti-rabies serum to prolong the incubation period while vaccine is given.

The indications for vaccine treatment, modified from the recommendations of the WHO Expert Committee on Rabies [this *Bulletin*, 1951, v. 48, 32] are outlined, as doctors are often in a dilemma as to whether prophylactic vaccine should be given in view of the possibilities of neurological complications.

The need for education of the community is stressed. A meercat which can be caught on the run is probably sick and therefore dangerous. Children should not pursue veldt animals or keep them as pets. In rural areas, people " should become meercat and wildcat conscious and look upon these animals as potentially dangerous ".

This is a very useful practical paper, of particular value to those in South Africa. *H. J. O'D. Burke-Gaffney*

Gremliza, L. Kasuistik zum Lyssa-Problem. [**Observations on Rabies**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1953, June, v. 4, No. 3, 382–9.

The English summary appended to the paper is as follows:—

" In a rural district of Persia, 32 persons were attacked and bitten by a rabid wolf, only 4 of which underwent effective anti-rabies treatment in the Teheran Pasteur Institute. 15 persons died of manifest rabies. Detailed case reports are given in order to determine the death rate for the 28 untreated persons. Mortality ran above 50 per cent. for persons bitten in face, scalp and neck region, and somewhat lower when the bites were on the upper extremity. Incubation period averaged 24 and 27 days after head and neck bites respectively, 45 days after arm and hand bites. It is pointed out that even severe laceration wounds caused by rabid animals do not necessarily lead to fatal consequences when left untreated. Similar conclusions are reached by Nikolic " [this *Bulletin*, 1952, v. 49, 946].

Garrido-Lecca, G. & Tola, A. **Complication of Rabies Vaccine Therapy treated with Corticotropin.** *Arch. Neurology & Psychiatry.* 1952, Nov., v. 68, No. 5, 605–8, 1 chart. [Refs. in footnotes.]

This paper gives a brief résumé of the main types of reaction—local and systemic—which complicate rabies vaccine administration. The main pathological changes are described and the incidence of such sequelae is discussed.

The case is described of a single white woman who suffered from paralysis and numbness of the legs and from dimness of vision after receiving 17 daily injections of anti-rabies vaccine administered on account of a bite on the leg by a rabid dog 3 days before treatment was begun.

The symptoms gradually became more severe, with increasing pain in the legs despite the administration of penicillin, streptomycin and terramycin followed by aspirin, phenobarbitone, vitamins and parenteral antihistamine.

Corticotrophin (ACTH) was then given in doses of 50 mgm. every 6 hours. After 48 hours there was marked improvement.

Eight days after the corticotrophin therapy was begun the patient's condition was almost normal and several months later she was leading her usual active life.

The authors enumerate hypotheses put forward to explain the occurrence of these systemic reactions; they accept the theory of an anaphylactic reaction first advanced by Harvey and McKendrick, and in view of the known anti-allergic action of corticotrophin suggest that this case proves that the mechanism of the complications involving the central nervous system is an anaphylactic reaction.

[In such systemic complications following the injection of anti-rabic vaccine the prognosis is generally good and complete recovery is not uncommon but in this case the rate of recovery after the exhibition of ACTH was remarkable and the method seems worthy of a thorough trial in centres where mammalian nerve tissue is still being injected as a carrier-medium for the vaccine virus.] *George R. McRobert*

Donatien, A., Poul, J. & Rampon, R. Essais de vaccination du chien par un virus rabique atténué. [**Trials of Vaccination of Dogs with an Attenuated Rabies Virus**] *Arch. Inst. Pasteur d'Algérie.* 1953, Mar., v. 31, No. 1, 71–4.

PLAGUE

Cavanaugh, D. C. & Quan, S. F. **Rapid Identification of *Pasteurella pestis* using Specific Bacteriophage lyophilized on Strips of Filter Paper. A Preliminary Report.** *Amer. J. Clin. Path.* 1953, June, v. 23, No. 6, 619–20, 1 fig.

In 1950, the WHO Expert Committee on Plague recommended that specific bacteriophage should be used in identifying *P. pestis* [this *Bulletin*, 1951, v. 48, 251]. The present authors, from California, now describe a rapid and simple method to this end which can be used in the field. An 18-hour broth culture of avirulent *P. pestis* (EVM) is incubated at 30°C. for 6 hours in heart infusion broth (Difco) and then 5 ml. of bacteriophage having a working titre of 10^{-4} [Gunnison *et al.*, this *Bulletin*, 1952, v. 49, 45] is added. After 18 hours, organisms are removed by Seitz filtration. Titres are usually found to be at least 10^{-4}: cultures are never completely lysed, in the authors' experience.

Three strips of filter paper, 0·5 × 3 cm., sterilized by steam pressure, are soaked in 0·5 ml. bacteriophage for 2 hours at room temperature, and then transferred to Pyrex tubes, to which they are allowed to adhere. They are then shell-frozen and lyophilized on a Stokes Cryochem apparatus: other strips are desiccated *in vacuo* over Drierite. The dried strips are sealed under nitrogen and stored at room temperature. The treatment causes a slight reduction in working titre.

The strips are applied to plates of blood agar heavily swabbed with 18-hour broth cultures and are gently pressed into place: untreated strips are used as controls. After 18–24 hours' incubation at 20°C. a 1 mm. zone of lysis is seen around the strips and this extends into the surrounding culture on prolonged incubation.

The method was used at 30-day intervals with 2 virulent strains (195/P and Yreka) and 4 avirulent strains (A1122, EV51, Tjiwidej and Tru) of

P. pestis. Up to 3 months later, all have shown zones of lysis. There was no activity against the strains of *Shigella* or *Salmonella* that had been found to show lysis by Lazarus and Gunnison [this *Bulletin*, 1947, v. 44, 1064] or against *P. pseudotuberculosis rodentium*. Desiccated slips are more easily prepared but do not keep as well as lyophilized strips.

The specificity of this procedure is being studied with many wild rodent strains of *P. pestis*. *H. J. O'D. Burke-Gaffney*

Burroughs, A. L., with the technical assistance of M. B. Britschgi. **Sylvatic Plague Studies. X. Survival of Rodent Fleas in the Laboratory.** *Parasitology*. 1953, May, v. 43, Nos. 1/2, 35–48. [33 refs.]

The longevity was investigated of 8 species of fleas, all taken from rodents known to contract plague under natural conditions in California, U.S.A.: *Xenopsylla cheopis* and *Nosopsyllus fasciatus* from Norway rats; *Opisodasys nesiotus* and *Malaraeus telchinum* from field mice; *Orchopeas sexdentatus sexdentatus* from wood rats; *Diamanus montanus* from California ground squirrels; *Megabothris abantis* from *Microtus longicaudus* and *Oropsylla idahoensis* from *Citellus beldingi*. All the fleas (10,795) used in the experiments were bred in the laboratory.

The author first reviews the literature on flea survival, then describes his laboratory conditions and lastly the experimental work, species by species, giving in tables the complete data for each experiment. Temperature, humidity, food source and frequency of feeds were varied in an attempt to obtain information on the potential length of life of a flea in its natural habitat. The maximum longevities recorded are:

	Maximum length of life in days by sex		
	Unfed	Fed once	Fed daily
Xenopsylla cheopis	40 ♂	41 ♂	158 ♀
Nosopsyllus fasciatus	13 ♂	22 ♂	281 ♀
Diamanus montanus	45 ♀	52 ♀	331 ♀
Oropsylla idahoensis	37 ♀	43 ♂	352 ♀
Opisodasys nesiotus	15 ♂	17 ♀	48 ♂
Malaraeus telchinum	15 ♂	20 ♀	182 ♀
Orchopeas sexdentatus sexdentatus ...	14 ♂	15 ♀	319 ♀
Megabothris abantis	10 ♂	19 ♀	477 ♀

The opportunity to obtain frequent blood meals had the greatest effect of any single factor in producing individual long-lived fleas. The longest-lived in all instances were those kept at 90 per cent. relative humidity or more and fed daily. *H. S. Leeson*

Tanaka, H., Sumiyoshi, K. & Kagioka, T. [**Studies on Rats in the Subway of the Osaka City**] *J. Osaka City Med. Center*. 1952, Apr., v. 1, No. 3, 208–9. [In Japanese.]

The English summary appended to the paper is as follows:—

"From the standpoint of public health, from May to June 1951, we studied on the rats in the subway of Osaka City.

"Of the total 122 rats collected in the Subway, 73 R.n. norvegicus 59·8%, 42 R.r. alexandrinus 34·5% and 7 R.n. var. hibernicus 7, 5·7%, and it is noted that the number of the female rats was greater than that of male in all species.

"Of the external parasites, X. cheopis was the most abundant and its parasitic index 1·97, this finding suggests the important role of the fleas for the epidemic, and other external parasites were less than in the other regions."

McCrumb, F. R., Jr., Mercier, S., Robic, J., Bouillat, M., Smadel, J. E., Woodward, T. E. & Goodner, K. **Chloramphenicol and Terramycin in the Treatment of Pneumonic Plague.** *Amer. J. Med.* 1953, Mar., v. 14, No. 3, 284–93, 9 figs. [22 refs.]

The authors describe the dramatic results of treatment of 13 cases of proved pneumonic plague by chloramphenicol, terramycin, and streptomycin, at Tananarive in Madagascar. Most of these cases have already been described or reported in papers by Girard [see this *Bulletin*, 1953, v. 50, 111] and by Mercier and MacCrumb [*ibid.*, 406].

The present paper, which is more complete and is well illustrated by charts, contains a comprehensive description of a very important advance in the treatment of pneumonic plague. Six of the patients were treated with chloramphenicol, given orally; 2 were treated with terramycin, orally; 3 with streptomycin, intramuscularly; and 2 with a combination of streptomycin and chloramphenicol or terramycin. There were only 2 deaths of patients whose treatment was started 40 and 24 hours after the onset; one was treated with chloramphenicol, the other with streptomycin. Every patient treated within 16 hours with any of the antibiotics made a rapid favourable response with early defervescence. The sputum became negative in 4–30 hours; in the fatal cases it became negative within 6 hours. Charts containing full details illustrate 5 of the cases.

Chloramphenicol and terramycin are regarded by the authors as being preferable to streptomycin on the grounds of lower toxicity, absence of resistance to the drugs, and greater effectiveness against secondary bacterial infection. The dosage recommended for each drug has already been stated in the papers referred to above. *John W. D. Megaw*

Garber, E. D., Noble, Kathryn & Carouso, N. **Genetic Studies on the Development of Streptomycin Resistance in** *Pasteurella pestis*. *J. Bacteriology*. 1953, May, v. 65, No. 5, 485–9, 2 figs.

The authors describe a study of the frequency with which streptomycin-resistant cells of *Pasteurella pestis* make their appearance in cultures grown on media containing concentrations of streptomycin ranging from 2 to 128 units per ml. The resistant forms are regarded as mutants of the normal bacilli and evidence was obtained that the number of these was so low that in natural infections, even with virulent strains of *P. pestis*, the few organisms arising as resistant mutants would not be likely to survive the defensive mechanism of the host. An example of the experiments was the seeding of 50 plates of tryptose agar containing 25 units of streptomycin per ml. with 1×10^8 viable organisms each from a highly virulent strain of *P. pestis*; altogether only 7 fully resistant colonies developed and of these only 3 were virulent for mice and guineapigs.

[But see this Bulletin, below, p. 934, which suggests that streptomycin resistance is of considerable practical importance.] *John W. D. Megaw*

Diagne, A., Michel, L., Koite, P. & Veyret, D. Sur l'emploi des dérivés de la coumarine comme raticides à Dakar. [**Trials of Coumarin Derivatives as Raticides at Dakar**] *Bull. Méd. de l'Afrique-Occidentale Française*. 1952, v. 9, No. 2, 273–99.

The anticoagulant coumarin derivatives tested were dicoumarol in the form of "Acavyl" issued by the Laboratoires Roussel and a proprietary article called "Tomorin" produced by the firm of Geigy and containing 1·0 per cent. of a coumarin derivative.

Good results were obtained with both preparations in 7 different localities or buildings; Acavyl was found most convenient, being supplied in powder form. A suitable strength was 1 gm. per 1,000 gm. of millet flour or other bait. The advantages claimed for coumarin derivatives are the absence of bait-shyness and the relative safety of the baits, but mention is made of the death of two cats in a storehouse in which Tomorin was dusted freely on the runs of rats so as to act as a contact poison. It was not known whether the cats died from eating poisoned rats or from licking the poison dust adhering to their paws and bodies.

In places where no immigration of fresh rats occurs complete disinfestation may be obtained in 2–4 weeks and where immigration occurs continuous baiting can be maintained. Absence of pulicide action is a drawback and a suggestion is made in the paper that a ring of powder containing 3 parts of Tomorin and 1 part of 10 per cent. DDT powder may be spread round each of the baits, or that this powder may be used in places where contact poisoning is suitable.

[Several proprietory powders and prepared baits of coumarin derivatives are now widely advertised for general use as raticides; these include Tomorin and Warfarin. Presumably dicoumarol powder, mixed with 1,000 times its weight of bait, would be fully effective.] *John W. D. Megaw*

McCrumb, F. R., Jr., Larson, A. & Meyer, K. F. **The Chemotherapy of Experimental Plague in the Primate Host.** *J. Infect. Dis.* 1953, May–June, v. 92, No. 3, 273–87, 10 figs. [36 refs.]

This paper contains a detailed description of an extensive study of experimental bubonic and pneumonic plague in monkeys (*Macacus rhesus*), with special reference to the effects of treatment with modern antibiotics.

Groups of monkeys were inoculated, either intracutaneously with about 3,000 million highly virulent plague bacilli or intratracheally with 1 to 100 million bacilli of the same strain. The animals were closely observed and quantitative blood cultures were made at frequent intervals. Treatment was started 36–48 hours after the onset of the illness so that the animals were already in a state of lethargy and dyspnoea, and in every case of bubonic infection bacteraemia was established; in the pneumonic cases there was evidence of pneumonitis observable by X-ray examination. The antibiotics were given in the same way as in the treatment of human patients.

After intracutaneous inoculation local signs appeared within 6 hours; fever and lymphadenitis occurred during the next 12 hours; the animals remained active for 24 to 48 hours after the onset of the fever. All the 20 control monkeys died, usually between the 60th and 84th hour of the illness. After intratracheal inoculation fever was the first sign; the incubation period was 1–3 days. Soon X-ray evidence of pneumonitis appeared and the animals became dyspnoeic on the 2nd day of the illness. The 10 control monkeys died about 4½ days after the onset.

Graphs showing the chief features of 9 cases are given. In bubonic cases bacteraemia was observed 18–36 hours after inoculation and in untreated cases the count rapidly rose, usually to at least 1,000 million per ml. In blood smears bacilli could not be detected till the count rose to 100,000 per ml. In pneumonic cases the bacteraemia was relatively slight—about 10 to 10,000 per ml. Very high leucocyte counts, reaching sometimes 75,000 or 150,000 per cmm. were not uncommon in the terminal stages of bubonic cases, but in pneumonic cases the numbers were much smaller and sometimes were normal, so that the progress of the illness in these cases was best judged by the degree of development of X-ray shadows in the lungs.

The usual therapeutic results were rapid defervescence, the temperature falling to normal within about 20 hours, and in 48 hours most of the treated animals became normally active. Blood cultures became sterile within 24 hours in 12 of the 16 treated monkeys of the bubonic groups and in all the 6 treated monkeys of the pneumonic series in which bacteraemia had developed before treatment was started.

The results of treatment are shown in the table below.

	Bubonic		Pneumonic	
	Recovered	Died	Recovered	Died
Aureomycin	3	3	–	–
Streptomycin	3	1	0	2
Chloramphenicol	6	0	3	2
Terramycin	–	–	0	2

The 3 monkeys that died after aureomycin had overwhelming bacteraemia when treatment was initiated; the counts were 120 to 146 million bacilli per ml. of blood and death occurred within 12, 18 and 60 hours respectively after the first dose was given. In the bubonic case in which streptomycin failed the initial bacteraemia was heavy—20 million per ml. There was another failure with streptomycin but recovery followed a change to chloramphenicol.

In the pneumonic cases one of the deaths after streptomycin was due to resistance to the drug, so there were two cases of streptomycin resistance in 6 treated. Of the 2 pneumonic cases fatal after chloramphenicol one had apparently made a rapid recovery but there was a relapse on the 17th day; in the other case bacteraemia had disappeared in 24 hours but death occurred 12 hours later. Terramycin appeared to cause a prompt recovery in the pneumonic cases, but both animals later became prostrate and died on the 10th and 11th days; this result was not explained; the drug is known to have caused dramatic cures in human cases [see above, p. 933].

Cortisone had no apparent effect in 5 cases in which it was given with a view to overcoming excessive bacteraemia; all the monkeys died in spite of treatment 20 hours later with chloramphenicol. Anti-plague globulin from hyperimmune rabbits also had no apparent effect in late stages of overwhelming infections, even when combined with chloramphenicol; on the contrary its intravenous injection appeared to cause sudden death in 4 of 5 monkeys, probably due to anaphylaxis.

Antibody formation in the course of the illness was studied; the rickettsia-agglutination reaction became positive earlier and at a much higher titre than complement-fixation; the maximum titres of both reactions were reached between the 10th and 20th days of infection. According to the illustrative chart the fixation test became negative, on the average, after 10 weeks and the agglutination test still showed an average titre of about 1 in 16 at this stage. A formolized suspension of the homologous strain of *P. pestis* was used in the agglutination test.

The original paper will repay perusal by everyone interested in plague, but, as the authors point out, the results observed cannot be regarded as reliable indications of the relative merits of the various antibiotics in the treatment of the disease in man. *John W. D. Megaw*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

Ricci, M. Ricerche parassitologiche nell'isola d'Ischia. IV. Note sul parassitismo intestinale nella popolazione adulta. [**Parasitological Studies on the Island of Ischia. IV. Intestinal Parasites in Adults**] *Riv. di Parassit.* Rome. 1953, Apr., v. 14, No. 2, 85–8.

The English summary appended to the paper is as follows:—

"The author reports the results of 81 examinations of feces from adults living at Ischia island.

"The index of infestation is shown to 83·95%. Of the people tested, 54·41% resulted positive for 2–4 species of parasites. The following 12 species were identified; and the percentages are given: *E. coli* (28·40%), *E. histolytica* var. *minuta* (4·94%), *I. bütschlii* (7·41%), *E. nana* (1·23%), *T. intestinalis* (1·23%), *R. intestinalis* (4·94%), *C. mesnili* (2·47%), *G. intestinalis* (3·70%), *H. nana* (1·23%), *A. lumbricoides* (18·52%), *N. americanus* (1·23%), *T. trichiura* (70·84%).

"The comparison between the present results and those obtained from the analogous research carried out on children of the very same centers, shows that there are no differences inasmuch as reported species, while positive differences exist in the diffusion of *E. coli*, which is more frequent among adults, and in *G. intestinalis* and *A. lumbricoides*, which is more frequent among children."

Hallman, Frances A. & DeLamater, J. N. **Demonstration of Amylolytic Activity in Cultures of** *Endamoeba histolytica*. *Exper. Parasit.* New York. 1953, Apr., v. 2, No. 2, 170–3, 2 figs.

It is well known that the growth of *Entamoeba histolytica* in culture is promoted by addition to the medium of starch granules, but up to the present the enzymes responsible for the assimilation of starch have not been demonstrated. In the present paper the authors describe the results of experiments devoted to the solution of this question. Agar plates in Petri dishes were prepared with "Bacto Blood Agar Base" to which 0·3 per cent. "Difco Soluble Starch" was added. Sterile porcelain "penicylinders" were then set into the cooled plate, and were used for growing miniature cultures of amoebae, which were inoculated together with antibiotics for the inhibition of bacterial growth. Identical penicylinder cultures were made from the flora accompanying each amoebic strain, the cylinders were covered with coverslips, and the Petri dish cultures were incubated at 37°C. for 48 hours. The penicylinders were then removed from the Petri dish and the agar plate was flooded with Gram's iodine. The presence of starch hydrolysis was shown by a clear area surrounding the culture site, whereas the rest of the plate was coloured blue from the iodine-starch reaction. By this method hydrolysis of starch was demonstrated in the case of all the amoebic strains used in the experiments, while

the bacterial controls did not affect the plates. It was also shown that the amylolytic substance elaborated by the amoebae diffuses into the solid phase of the medium. *C. A. Hoare*

Everritt, Martha G., Sadun, E. H. & Carrera, G. M. **Cultivation of *Endamoeba histolytica* in the Chick Embryo.** *Exper. Parasit.* New York. 1953, Apr., v. 2, No. 2, 141–6, 1 fig. [15 refs.]

Entamoeba histolytica, originating from cultures or from human stools, were treated with antibiotics (penicillin and streptomycin) in order to inhibit the concomitant bacteria, after which the amoebae were inoculated on the chorio-allantoic membrane and into allantoic, amniotic and yolk-sac cavities of 8- to 12-day chick embryos. After incubation at 37°C. for varying periods the tissues and fluids were examined—directly and by subinoculation in a culture medium containing *Corynebacterium*—for the presence of amoebae. These were also sought for in sections of chick tissues.

The results of these experiments were as follows. In the case of chorio-allantoic inoculations, two-thirds of the embryos were dead after 2–6 days, without showing any amoebae, though these survived up to 12 hours. In the case of allantoic inoculation most of the embryos also died, but in 2 of the dead ones amoebae were seen. In the case of amniotic inoculations, many were positive up to 72 hours though a large proportion of the embryos were dead. However, the amoebae failed to grow in the yolk sac. No evidence was produced of multiplication of the amoebae or of penetration of the embryonic tissues. It is thought that the mortality among the inoculated embryos was due chiefly to insufficient inhibition of the accompanying bacteria. The paper is illustrated by a photomicrograph.

C. A. Hoare

Bradner, W. T. **A Study of the Physiology of Bacteria which support the Growth of *Endamoeba histolytica in Vitro*.** *J. Parasitology.* 1953, June, v. 39, No. 3, 326–31. [14 refs.]

It had not been possible to culture *E. histolytica* in the absence of bacteria or their products till Phillips [this *Bulletin*, 1950, v. 47, 624, 741] successfully employed *T. cruzi* for this purpose. The use of such cultures after death of the trypanosomes under experimental conditions provides a suitable means of studying the growth of *E. histolytica* in association with different added organisms. The method appears to possess advantages over those formerly employed in which washed sterile cysts, amoebae from sterile liver abscesses or trophozoite cultures freed from accompanying bacteria by antibiotics were used as a source of culture material. The physiology of organisms supporting amoebic growth has been systematically studied in the present investigation in the hope that light might be thrown on the growth requirements of amoebae.

Three different strains of *E. histolytica* were used and aerobic as well as anaerobic organisms were included in the 65 bacterial types tested. Cleveland's liver-infusion agar overlaid with serum-saline plus rice starch was the medium employed. After incubation of the particular bacterium for 24 hours at 37°C. in this medium 0·5 ml. of a Phillips's culture with each of the 3 strains of amoeba was inoculated and incubation was continued for 4 days at 37°C. and longer if necessary to establish the presence or absence of amoebae. In successful cases serial transplants were made to prove that

growth and multiplication of amoebae occurred. Tubes with organism "t", which is known to support growth of amoebae, were used in each experiment as controls, but sometimes failed to produce good growth in one of the strains of *E. histolytica* used.

The physiological characters of 8 bacteria which supported continued growth of *E. histolytica* were studied in different media and compared; 6 of them are reported as possessing this property for the first time. Seven other bacteria were found to support growth on a limited number of occasions. The remaining bacteria tested proved unsuitable.

The results indicated that a wide difference existed in the ability of different strains of the same species to support amoebic growth and in the same way different strains of amoebae failed to grow in presence of the same bacterium. It is suggested that these facts might be turned to practical account in identification tests. The physiological characters of the supporting bacteria are recorded in a table. It is pointed out that none fermented adonitol or dulcitol or produced indole or acetylmethylcarbinol.

J. D. Fulton

Abdine, F. H. & Youssef, A. S. **Needle Biopsy in the Diagnosis of Liver Disease in Egypt.** *J. Roy. Egyptian Med. Ass.* 1953, v. 36, No. 3, 217–35, 7 figs. [11 refs.]

Liver biopsies were performed on some 160 patients, with a Silverman needle; the needle was introduced intercostally unless there was marked liver enlargement, when it was introduced subcostally. There were two fatalities from haemorrhage as a result of the procedure, and another probably due to misdirection of a needle into an empyaemic gall bladder containing stones.

In none of 10 cases of suspected amoebic hepatitis were the findings diagnostic, and no amoebae were found in the material obtained. Ova were recovered by this means from only 20 of 42 cases of suspected schistosomiasis of the liver; in another 6 such cases the histological appearances were considered to be diagnostic of the condition. Brief descriptions are given of the findings in other conditions, including infective hepatitis, cirrhosis probably of nutritional origin, pellagra, diabetes and neoplasm. *A. R. D. Adams*

Blanc, F. & Navaranne, P. Les splénopathies amibiennes. [**Amoebic Splenomegaly**] *Arch. Méd. Gén. et Trop.* 1953, Mar.–Apr., v. 30, No. 2, 45–56. [39 refs.]

This is an account of 3 patients from malarious areas, with splenomegaly. The considerable splenomegaly was held largely to be due to an amoebic splenitis, as it resolved under treatment with emetine. The possible routes of infection of the spleen are considered.

[No proof of any *Entamoeba histolytica* infection in any of the three patients was forthcoming.] *A. R. D. Adams*

Sloan, S. & Freedman, T. **Aspiration and Air Replacement in Diagnosis and Management of Amebic Liver Abscess.** *Arch. Intern. Med.* 1953, Apr., v. 91, No. 4, 550–55, 3 figs. [Refs. in footnotes.]

"The case of a patient with a large amebic liver abscess, treated with aspiration, emetine, chloroquine and aureomycin is presented. The use of aspiration followed by injection of air into the abscess cavity is suggested as an aid in the diagnosis, therapy, and prognosis in selected cases. Current methods of treatment of amebic liver abscess are outlined."

Oliver-González, J. & Dobal, J. M. **Treatment of *Endamoeba histolytica* Infections in Man with Fumagillin.** *Bol. Asoc. Méd. de Puerto Rico.* 1953, Apr., v. 45, No. 4, 127–30.

The authors, in Porto Rico, gave fumagillin to 28 persons in oral doses of 10 to 30 mgm. daily for 10 days: 26 were carriers of *E. histolytica* cysts and 2 were suffering from amoebic dysentery and passing trophozoites. Stools were examined by direct and concentration methods daily during the course and thereafter weekly during the period of observation.

The results are shown in a table and may be summarized as follows:—

Cyst-passers

Fourteen persons were given 30 mgm. daily: 12 were negative for cysts in 2 to 4 days and remained negative for 92 days. Six were given 20 mgm. daily: all were negative in 1 to 3 days and remained so for 280 days. Six were given 10 mgm. daily: 4 were negative in 2 days and remained so for 271 days; the other 2 were positive on the 24th and 31st days.

Thus, 22 of 26 were negative for 92 to 280 days.

Passers of trophozoites

Two received 30 mgm. daily: the stools became negative in 3 and 5 days and remained so for 265 days. There was marked clinical improvement. These patients were apparently cured by a single course.

No serious reactions were noted. Some patients had transient anorexia and headache during the first 3 days. A patient who developed pruritus ani and muscular pains was shown to have been hypersensitive to streptomycin and penicillin.

The authors refer to the findings of Killough *et al.* [this *Bulletin*, 1952, v. 49, 696] that fumagillin is essentially non-toxic in doses up to 50 mgm. daily for 2 weeks. In their own series, 30 mgm. daily appeared to be adequate, but they rightly point out that this experience is confined to 2 patients only. They suggest that therapeutic response to fumagillin may vary with different topographical strains of *E. histolytica*. [See also Anderson *et al.*, this *Bulletin*, 1952, v. 49, 1121.]

H. J. O'D. Burke-Gaffney

McHardy, G., Bechtold, J. E., Welch, G. E. & Browne, D. C. **Fumagillin as an Amebacide. Preliminary Report.** *Southern Med. J.* 1953, May, v. 46, No. 5, 428–32. [18 refs.]

Claims originally made as to the efficiency of aureomycin as an amoebicide have not been substantiated; it is now agreed that aureomycin and terramycin act in amoebiasis by reason of their effect on the bacterial symbionts in the bowel necessary to the survival of the amoebic infection. Fumagillin, which was prepared from *Aspergillus fumigatus* in 1949, has been shown *in vitro* to exert a directly amoebicidal action, though to have but very little antibacterial or antifungal effect [this *Bulletin*, 1951, v. 48, 640]. Studies *in vivo* have shown it to be remarkably devoid of toxicity and to exert an effective amoebicidal action in experimentally infected animals.

In earlier trials fumagillin in doses of 10 mgm. daily by mouth for 12½ days proved innocuous to man [this *Bulletin*, 1952, v. 49, 1121]; but 50 mgm. daily sometimes causes vertigo and anorexia [*ibid.*, 696]; 200 mgm. daily is said to produce "a papular-pustular dermatitis, nausea and emesis".

The present authors gave 10 student volunteers 10 mgm. of the drug daily, and later increased this by 10 mgm. increments each day to a maximum of 100 mgm. daily. At the 30 mgm. daily dose there was anorexia; at 60 mgm. nausea and abdominal discomfort; and in one case at 90 mgm. emesis. There was slight temporary diarrhoea in 2 cases at 70 mgm. and 8 of the volunteers suffered from vertigo at and above the 60 mgm. dosage. No skin changes were observed, and renal, hepatic and blood estimations showed no deviations from the normal.

Sixty-four patients with proved intestinal amoebiasis were treated with fumagillin given orally in doses of 20 mgm. thrice daily for 10 consecutive days. Some minor side effects, insufficient to interfere with the treatment, were noted. The patients were observed for as long as possible after treatment; 18 were re-examined for 8 months, 22 for 6 months and the rest for at least 4 months thereafter. There were 3 parasitic relapses within these periods; though the other patients remained apparently parasite-free the authors stress the undesirability of making claims of cure until after much longer periods of observation. It was observed that those patients with concurrent infections with *Trichomonas*, with *Giardia* and with *Trichuris* apparently were freed of their parasites by the fumagillin treatment; *Ascaris* and *Strongyloides* infections were not affected by it.

A. R. D. Adams

Molina, A. Un antibiótico amibicida: Fumagilina. Terapéutica oral y atóxica de la amibiasis intestinal. [**Therapeutic Action and Non-Toxic Action of Fumagillin Given by Mouth in Intestinal Amoebiasis**] *Medicina*. Mexico. 1953, Mar. 25, v. 33, No. 672, 132–6, 4 figs. [10 refs.]

A review of the literature.

Leal, R. A. & Amaral, A. D. F. Aglutinação de trofozoítos de uma endameba de vida livre (*E. moshkovskii*) por sôro sanguíneo humano. [**Agglutination of *Endamoeba moshkovskii* Trophozoites (a Free Living Organism) by Human Blood Serum**] *Arquivos Facul. de Hig. e Saude Pública. Univ. de São Paulo*. 1952, June–Dec., v. 6, Nos. 1/2, 1–7, 3 figs. on pl. English summary.

Entamoeba moshkovskii [see this *Bulletin*, 1953, v. 50, 29] is a free-living amoeba isolated from sewage. It was cultivated in Amaral's liquid medium as described by him in 1945 (*An. Fac. Med. Univ. S. Paulo*, v. 21, 175). Two strains were used and after cultivation for 2–4 days the growth was filtered to remove larger particles. The filtrate was centrifuged at 1,500 r.p.m. for 3–5 minutes, the supernatant was poured off and the deposit washed and centrifuged twice in physiological saline and the trophozoites in the residue used for the agglutination tests. The human serum for the tests was obtained from normal subjects and from others with *E. histolytica* infection. Serum and culture were mixed in equal amounts of 0·1 cc. with a glass rod on a well-slide and placed at 37°C. for an hour and examined with objective 10, ocular 12. Controls were set up with physiological saline. Sera from 20 persons were thus tested and agglutination was observed in 5–10 minutes and lysis in 15–45 minutes. If the serum was inactivated at 56°C. for half an hour, the agglutination was still present at laboratory temperature or at 37°C., after being kept for 24 hours in the ice-chest at 2–8°C., and the amoebae were not disintegrated.

Next, various dilutions of serum were tried in 10 cases and agglutination

was observed up to 1:20 in one person whose faeces showed nothing pathogenic; positive at 1:20, doubtful at 1:40 in another with *E. histolytica*, *E. coli* and *E. nana*, in the faeces; 2 (and a third doubtful) were positive at 1:320. In some no agglutination was seen until after a stay of 24 hours in the ice-chest. None of those with *E. histolytica* infection agglutinated higher than 1:160 and only one as high as this; others did so at 1:20 and 1:40. There is, therefore, no correlation between the agglutination of this free-living amoeba and the presence of *E. histolytica*. The details are set out in a table. *H. Harold Scott*

RELAPSING FEVER AND OTHER SPIROCHAETOSES

Fischer, L. Zur Frage des Rückfallfiebers in Afghanistan. [**Relapsing Fever in Afghanistan**] *Ztschr. f. Topenmed. u. Parasit.* Stuttgart. 1953, June, v. 4, No. 3, 339–43. 3 charts. [22 refs.]

The English summary appended to the paper is as follows:—

"A well observed case of relapsing fever in Afghanistan is reported. It was doubtful whether the infection was caused by ticks or by lice, both of which are potential transmitters of relapsing fever in the Middle East, probably carrying varied spirochete strains. The scarcity of spirochete findings indicated a tick bite fever and contrasted with the clinical course leading to relapses 3 and 8 weeks after the original fever. Persistent circulatory instability was a dominant symptom."

Vaisman, A., Hamelin, A. & Levaditi, C. Spécificité des immobilisines récurrentielles entre le *Borrelia duttoni* et le *Borrelia hispanica*. [**Specificity of Immobilizing Antibodies of** *Spirochaeta duttoni* **and** *Sp. hispanica*] *Ann. Inst. Pasteur.* 1953, Apr., v. 84, No. 4, 774–7.

Continuing their investigations of immobilizing antibodies [this *Bulletin*, 1953, v. 50, 219, 310], the authors claim to be able to differentiate between *Spirochaeta duttoni* and *Sp. hispanica* by demonstrating the presence of specific antibodies in rats and mice infected with these 2 species.

J. C. Broom

Charmot, G., le Henand, F. & Giudicelli, P. La terramycine dans le traitement de la spirochétose dakaroise. [**Terramycin in the Treatment of Relapsing Fever in Dakar**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 295–6.

Reports of the action of terramycin in experimental relapsing fever [this *Bulletin*, 1953, v. 50, 815] encouraged the authors to try this antibiotic in the treatment of patients with the disease.

They point out that the clinical form of relapsing fever in Dakar is predominantly meningeal, but note that clinical records have shown that terramycin, although it does not easily pass the healthy meningeal barrier, is effective in bacterial meningitis, and therefore might be in relapsing fever. They have treated 10 Europeans suffering from confirmed tick-borne relapsing fever of this type. The average dose of terramycin was 3 gm. daily for 5 days, then 2 gm. daily for the next 5 days. ...

In every case the results were excellent: pyrexia disappeared in 1 to 3 days, no relapses occurred [observation period not stated], mouse inoculations remained negative. Tolerance to terramycin was good. The authors conclude that this treatment was superior to arsenicals and penicillin and equal in value to aureomycin: but they do not suggest that it should replace aureomycin in the treatment of relapsing fever, as their primary object was to test the extent of the efficacy of terramycin in tropical diseases in general. *H. J. O'D. Burke-Gaffney*

YAWS AND OTHER TREPONEMATOSES

Edmundson, W. F., Lopez Rico, A. & Olansky, S. **A Study of Pinta in the Tepalcatepec Basin, Michoacan, Mexico. I. Field Identification of the Disease.** *Amer. J. Syph.* 1953, May, v. 37, No. 3, 201–6. **II. Mass Survey Considerations.** *Ibid.*, 207–12. **III. Survey Results and Interpretation.** *Ibid.*, 213–20. **IV. Serologic Findings in a Survey.** *Ibid.*, 221–5, 3 figs.

I. A Centre of Epidemiological Studies has been established in the town of Apatzingan in the Tepalcatepec Basin. This area is semi-arid with an annual rainfall of 7–9 inches (200 mm.) during 4 months. It is from 984–9,842 feet (300–3,000 metres) above sea level. The population is mainly of American-Indian and European mixed stock; living and sanitary conditions are underdeveloped. The most important diseases are malaria, pinta (*mal del pinto*), intestinal infections and parasitism, goitre, tuberculosis and malnutrition. Most of the 250,000 (estimated) cases of pinta in Mexico occur in the valley of the Balsas river; the Tepalcatepec river is its chief tributary.

"Pinta is principally a disease of the skin which generally causes no disability or serious physical handicap. No acceptable proof has been presented that it causes symptoms other than the manifestations seen on the body surfaces." In endemic areas the disease is not a disability but in pinta-free areas it is a socio-economic handicap since it is believed to be contagious, and anguish and psychological reactions may be caused.

The treponemal origin of the disease was recognized in 1938. Its relation to other treponematoses and its mode of transmission are not at present fully understood.

The relatively isolated village of Capirio comprises 54 families of 256 persons; 121 of these were studied. The exposed parts of the body were examined; this had been shown, in another village, to allow of accurate diagnosis. A number of serological tests for syphilis (STS) [Mazzini qualitative, Kahn quantitative and qualitative, VDRL slide quantitative and qualitative, and Kolmer (cardiolipin) quantitative], the *Treponema pallidum* immobilization test (TPI) and dark-field examination were also carried out.

All except 2 persons with positive STS had definite clinical manifestations of pinta. Of 44 patients on whose sera the TPI test was carried out, in 28 the TPI and STS tests were positive and clinical evidence of pinta was present; in 8 the TPI and STS tests were positive but no clinical examinations had been made, in 6 these three items were all negative and in 2 there was disagreement in the TPI and STS tests and no clinical evidence of pinta was present.

The accuracy of the diagnosis of pinta by the patients themselves or older members of the family was checked against that of a dermatologist with only 4 errors in 64 persons. It was found that 39 of the 54 families had living members who gave a history of pinta; in 12 families (30 per cent.) half or less of the members and in 27 families (70 per cent.) more than half of the members gave histories of pinta; in 11 of these 27 families all members said they had pinta.

II. In the previous paper " it was established by an analysis of clinical and serologic findings that pinta could be identified with reasonable accuracy by examination of the exposed surfaces of the body ". Two other isolated communities were surveyed to assess the value of " diagnoses made by examination of exposed body surfaces as a mass case-finding method ". Special attention was paid to children since pinta is most frequently acquired in childhood and serological reactions in them would be less likely to be due to syphilis, which is more frequently acquired in adolescence or later.

The exposed skin surfaces of 238 persons were examined and blood specimens were collected from them. Blood was also taken from persons with no clinical evidence of pinta. Of 163 persons who had received no previous treatment clinical evidence of pinta was found in 16; of these 11 were STS positive, 2 doubtful and 3 negative. Of the 147 persons who had no pinta, 139 were STS negative, 2 positive and 5 doubtful [this adds up to 146]. The authors say that this supports " the contention that untreated seropositive nonclinical pinta (latent pinta) is either nonexistent or extremely uncommon ".

" There is no way of making the differential diagnosis serologically between syphilis and pinta." It is assumed that positive serological reactions in persons with no clinical evidence of pinta and who had received no previous treatment are either due to syphilis, biologically false positive reactions or to previously treated pinta that was denied by the patient.

Pinta lesions may occur in about 1 per cent. of patients on unexposed surfaces only.

" Control of pinta in a given population would seem possible if all patients with clinical evidence of pinta were treated adequately. There does not seem to be a sizeable reservoir of infection with pinta which is not detectable clinically with relative ease. Reinfection of the population group could be avoided by extending treatment activities in ever-widening circles along routes of communications, continued vigilance for new patients appearing in the treated area, and adequate re-treatment of relapsing patients." .

III. A survey was made of 198 of the 820 inhabitants of the rural town of Cenidor, the population of which is expanding. It is only 13 miles (21 kilometres) along a paved highway from Apatzingan where syphilis is a public health problem.

It was found that among persons with no clinical evidence of pinta those under 16 years of age gave fewer positive serological reactions than those over 16 years of age.

Whether any of these 198 persons had received any previous treatment was disregarded. Of 47 with clinical evidence of pinta 36 were serologically positive; of 151 with no clinical evidence of pinta on exposed parts 120 were negative and 21 positive serologically. The interpretation of the positive reactions in these 21 persons is discussed under the following heads: (1) latent pinta, which must be very infrequent, (2) residual sero-resistance following adequately treated pinta, which was probably present in some cases but could not be accurately determined, (3) pinta with lesions only

on unexposed parts of the body in possibly about 1 per cent. of pinta cases or misdiagnosed cases, (4) biologically false positive reactions but no evidence was found that these were frequent, (5) syphilis, which was regarded as accounting for most of them, or (6) treponematoses other than pinta or syphilis, of which none was present in the area concerned.

Pinta was found to be a rural disease contracted mainly in childhood as are yaws and several forms of endemic syphilis. Skin-to-skin contact is probably one method of transmission. There is no evidence of congenital pinta or of lesions comparable with the late lesions of syphilis. Syphilis is " considered relatively common " in these rural communities where pinta is highly endemic. It is known that a patient with pinta may acquire syphilis and *vice versa*.

In mass surveys the authors consider that clinical examination of exposed skin surfaces without serological examination is adequate for the diagnosis of pinta. Re-survey and treatment should be " done periodically ". " We believe that pinta is deserving of large-scale control efforts, even though it does not generally cause disabling or killing effects." The social and psychological consequences of pigmentary changes are regarded as adequate reasons for this. [The reviewer would have thought that the other diseases prevalent in the area, namely, malaria, intestinal infections and parasitism, goitre, tuberculosis and malnutrition, would individually and collectively have had greater calls on finance and man-power than pinta unless the control of pinta is to be made the means of improving the rural health services as is now the recognized purpose of yaws control measures. No reference, however, is made to this.]

IV. Serological studies showed that in pinta the titres of reactions remained at fairly constant, moderately high levels with the passage of time as indicated by the results in increasing age groups. This is contrary to the fall in titre usually observed in syphilis. The authors found that under field conditions the Mazzini (with lipoid antigen) test was adequate for screening purposes.

[There is much of interest and value in these 4 papers but they could, with advantage, have been combined in a single paper.] *C. J. Hackett*

Hackett, C. J. **The Principles and Practice of Yaws Control.** *Brit. Med. J.* 1953, July 11, 74–6.

This paper summarizes briefly the principles and practice of yaws control, and is based upon present knowledge and illuminated by the author's wide knowledge and experience of the subject in many lands.

In stating the principles, emphasis is laid on the importance of eradicating the disease rather than reducing it to a low endemic level, and on the necessity of including in the original plan post-campaign measures aimed at improving rural health services. The effort and cost involved in an intensive yaws campaign can only be justified by the steady development of these services. The post-campaign measures include the establishment of rural dispensaries with locally recruited itinerant staff, at which treatment of yaws cases is provided after the campaign and from which surveys of the neighbouring population may be made periodically in order to detect and treat fresh cases and to prevent spread if yaws is reintroduced. Other diseases also would be attacked by the staffs of these dispensaries, particularly the locally important diseases for which specific treatment can be given. Later, as therapeutic work decreases, preventive work would become their important function.

In discussing the application of these principles it is pointed out that the recent introduction of procaine penicillin in aluminium monostearate (PAM) gives such rapid and satisfactory results in the treatment of yaws that mass campaigns aimed at eradication may be undertaken confidently. A prerequisite of the campaign is an accurate census. The whole population is examined in order to detect all infectious and potentially infectious yaws cases, either by collecting the inhabitants of the area at a central point or by house-to-house visiting if the population is sparse and dispersed. Treatment is given immediately to those requiring it, preferably PAM in a dose of not less than 1·2 mega units in a single injection for an adult. Contacts of infectious cases should be given half the therapeutic dose as preventive treatment. Latent secondary stage cases are difficult to diagnose and suggestions are made by which most of them may receive treatment. The campaign has an educational value which should be continuously reinforced by specific activities in the field of health education. *T. H. Davey*

LEPROSY

WADE, H. W. **The Classification of Leprosy. A Proposed Synthesis based Primarily on the Rio de Janeiro-Havana System.** *Internat. J. Leprosy.* New Orleans. 1952, Oct.–Dec., v. 20, No. 4, Pt. 1, 429–62, 3 figs. [58 refs.]

The author begins with a description of the history of efforts to arrive at a scientific, practicable, and, as nearly as possible, generally acceptable classification. Recently, as president of the International Leprosy Association and editor of the *International Journal of Leprosy* he sent out to a number of leprologists a memorandum representing the draft of an article on classification. The memorandum contained 8 propositions on which correspondents were asked to give their views. The answers to this memorandum are analysed in the current number of the *International Journal of Leprosy* and the article under review is an attempt at a synthesis of the views expressed. A scheme is drawn up based primarily on the fundamentals of the South American system but with place also given to certain features of the system adopted in 1938 at the 4th International Congress held in Cairo. Six classes are listed, 4 of these being denominated " first class " and two as " subordinate class ". They are as follows :—

1. Lepromatous type (L) (a first-order class)
   (Varieties not distinctive; diffuse and Lucio forms mentioned; lepromatous and polyneuritic (LP) cases recognized; recessive and residual cases to be distinguished.)
2. Tuberculoid type (T) (a first-order class)
   Minor tuberculoid (Tm) torpid variety
   Major tuberculoid (TM) torpid variety
   Reactional tuberculoid (TR) variety
   (TP cases occur. Ulcerative " lazarine " cases are recognized, an infrequent variety. Recessive and residual cases to be distinguished.)
3. Indeterminate group (I) (a first-order class)
   (Subgrouping possible on histological grounds, but not important; no IP cases.)

4. Borderline group (B) (a first-order class)
   (A variety nearer the tuberculoid)
   (A variety nearer the lepromatous)
   (BP cases recognized; recessive and residual cases to be distinguished.)
5. Maculo-anaesthetic group (MA) (a subordinate class)
   (No subdivisions; MAP cases recognized.)
6. Polyneuritic group (P) (a subordinate class)
   Primary polyneuritic (P′) subgroup
   (Certain varieties possible)
   Secondary polyneuritic (P″) subgroup
   (Varieties according to previous form of disease.)

It is hoped that, with the preliminary clarification of the symposium and this article, it may be possible at the VI International Leprosy Congress to arrive at a satisfactory agreement on the classification of leprosy which will be acceptable throughout the world. *Ernest Muir*

Doull, J. A., Gray, H. H. & Bancroft, Huldah. **A Note on the Recorded Deaths from Leprosy, Continental United States, 1933–1948.** *Internat. J. Leprosy.* New Orleans. 1952, Oct.–Dec., v. 20, No. 4, Pt. 1, 463–6.

In the United States practically all death certificates on which leprosy is mentioned are classified under "leprosy" no matter what the actual cause of death may have been. During the 16-year period 1933–48 there were 451 deaths so classified. Leprosy is indigenous chiefly in Louisiana, Texas and Florida. Most of the deaths (86·7 per cent.) occurred in the National Leprosarium at Carville. The risk of dying from leprosy—and probably of contracting it—is as great or greater for Whites as for Negroes. The average age of patients dying at Carville for 1929–35 was 39·2 years, for 1943–50 it was 43·2. From 1933 to 1940 the average annual number of deaths attributed to leprosy in the United States was 31·0; for the 8-year period from 1941 to 1948 it was 25·4. These and other statistics give evidence of improvement which is probably attributable to the new forms of treatment, especially the sulphones. *Ernest Muir*

Gray, H. H. & Bancroft, Huldah. **Tuberculosis at the United States Public Health Service Hospital, Carville, Louisiana, 1922–1950.** *Internat. J. Leprosy.* New Orleans. 1952, Oct.–Dec., v. 20, No. 4, Pt. 1, 467–78.

At the National Leprosarium, Carville, U.S.A., the records from 1922 to 1950 were examined. It was found that tuberculosis was a common cause of death. During the period 1936 to 1942 there was a yearly average of 82·3 deaths per 1,000 patients, and 21·7 of them were attributed to tuberculosis. But during the years 1943–50, after the introduction of sulphone treatment, the average of deaths per 1,000 fell to 44·4, of which only 7·5 were attributed to tuberculosis. It is concluded that not only has the number of deaths diminished since the introduction of sulphones, but the average death from tuberculosis has diminished even more. *Ernest Muir*

Bermann, R. Essais de coloration du bacille de Stefansky et du bacille de Hansen par le noir Soudan B.N. [**Trials in Staining the Stefansky Bacillus and the Hansen Bacillus with Sudan Black B.N.**] *Bull. Acad. Nat. Méd.* 1953, v. 137, Nos. 19/20, 295–8.

It was found that the bacilli of about 80 per cent. of cultures of tubercle bacilli were stained with Sudan Black B.N. if before making smears the

bacilli were suspended in 100 per cent. alcohol. Differentiation was made by applying acetone, the stain still persisting in the bacilli up to 6 hours after application. When the same technique was used with Stefansky's bacillus, it was found necessary to apply the stain 2 to 4 times in order to get staining. The same was found to be the case with cultures of other acid-fast bacilli. In contrast with this, all attempts to stain the leprosy bacillus proved negative. The author takes these results as evidence confirming the opinion of Chaussinand [this *Bulletin*, 1949, v. 46, 147] that Stefansky's bacillus has more affinity with the tubercle than with the leprosy bacillus. *Ernest Muir*

Cleve, E. A. & Pruitt, F. W. **Alopecia Leprotica: its Relationship to Transmission of Leprosy.** *J. Amer. Med. Ass.* 1953, June 13, v. 152, No. 7, 573–7, 5 figs. [Refs. in footnotes.]

The authors found that the incidence of leprotic alopecia varied in different countries. The percentage of this condition among patients examined in leprosaria in Japan was 45·5, and the corresponding figures in Korea, Formosa, and among Chinese soldiers were respectively 29·44, 22·11 and 28·95. Statistics from 11 other countries give an average incidence of less than 0·3 per cent. The authors attribute the far greater incidence in the former countries to the Buddhist habit of shaving the scalps of newborn children repeatedly during the first few months. They argue thus: "The scalp invasion among the natives of Japan, Korea, and Formosa might theoretically be due to a greater virulence of the organisms, lesser resistance of the scalp, or greater dosage of the organism. These possibilities appear unlikely. . . The common factor in all cases appears to be the larger dosage of the organism, for trauma (including shaving) with complete removal of the natural protecting barrier of the hair and the inevitable production of small nicks and cuts would appear to predispose to heavy infection. It is clear that scalp infection is external in origin and not vascular from a central focus".

[No reason is given for this last statement. It would be strange indeed if vascular infection took place from a central focus to all other parts of the skin as far as the neck (and there is much evidence that it does) but avoided reaching the skin of the scalp. The authors say nothing about whether or not the scalp is infected in cases in which alopecia does not occur. As a matter of fact alopecia occurs fairly frequently in advanced lepromatous cases in India but not nearly as frequently as in Japan; but in many such cases in which there is no noticeable alopecia one finds on examination by smears or biopsy that there is gross infection of the scalp. It would seem that there is a fourth possible cause of leprotic alopecia in Japan, namely the ability of the hair follicles of the scalp to resist the pressure of the lepromatous process which surrounds them. Is it not a well-known fact that in some of the Mongolian races hair follicles are less strongly developed than in other races?]

A further argument of this paper is that "contraction of leprosy by healthy adults is rare, and most reported cases are open to question".

[This ignores the many known cases of people who have lived only in non-endemic countries till adult age, but have contracted leprosy later after spending years in endemic countries. The fact is well known that, as the authors say, "leprosy is contracted by an infant through skin-to-skin contact with a leprous person" but it is a dangerous theory, and one not

supported by facts, that contraction of leprosy by healthy adults is rare in endemic countries, or that it is open to question in most cases.]

Ernest Muir

Azulay, R. D. & Cezar de Andrade, L. M. **The Diagnostic Value of Lipoid in the various Structural Types of Leprosy. Observation of 1053 Cases.** *Internat. J. Leprosy.* New Orleans. 1952, Oct.–Dec., v. 20, No. 4, Pt. 1, 479–83.

A histological examination was made of 1,053 samples of skin of leprous patients; Sudan III or Scharlach R were used as a stain for lipoids. Lipoids were present only in lepromatous cases, though they were absent in 5 per cent. of non-regressive cases. In cases with simple inflammatory infiltration they were absent. They were absent from all tuberculoid cases even those that were reacting; indeed the authors consider that if lipoid is found in the skin of an apparently tuberculoid case it is a sign that it is becoming lepromatous. Under sulphone treatment the Virchow cells linger on after the bacilli have disappeared.

Ernest Muir

Aono, G. **A Hemolytic Reaction of Erythrocytes sensitized with Tuberculin and Components extracted from Leprosy Nodules.** *Tohoku J. Exper. Med.* 1953, Apr. 25, v. 57, No. 4, 311–15.

The author has used, as a test in leprosy patients, the haemolytic modification of the reaction of Middlebrook and Dubos, in which erythrocytes sensitized by tuberculin are haemolysed when placed in contact with serum from tuberculous patients. He also modified it by sensitizing the erythrocytes with extracts of leprosy bacilli prepared from leprosy nodules by a long and complicated process which is set forth in a table. Of 40 sera from patients with lepromatous leprosy 12 showed haemolysis in dilutions of 1 in 10 to 1 in 100, as did 5 of 25 with neuro-macular leprosy. These results are lower than in tests performed on tuberculous patients. Results with the haemagglutination test were similar.

With erythrocytes sensitized by extracts from leprosy nodules the results were all negative.

Ernest Muir

Lowe, J. & McNulty, F. **Tuberculosis and Leprosy. Immunological Studies.** *Leprosy Review.* 1953, Apr., v. 24, No. 2, 61–90. [40 refs.]

The authors begin with a brief history of the use of BCG in connexion with leprosy by Latin American and French workers. They then describe the lepromin test and the nature of its positive response, concluding that it is allergic but not specific. They next study variations in the results of the lepromin test in the same person from time to time, showing that, though the degree may vary, actual positivity and negativity seldom change. The work of Chaussinand [this *Bulletin*, 1949, v. 46, 1052; 1951, v. 48, 937] is quoted as showing that " patients with tuberculoid (allergic) leprosy, free from tuberculous infection, react strongly to the intradermal injection of Koch's bacillus killed by heat, while healthy people with lepromatous (anergic) leprosy show no such reaction ". In contrast with the persistence of the lepromin test, positive tuberculin results, both when induced by ordinary infection with tuberculosis and when induced by BCG vaccination, are often short-lived. The authors then describe methods of preparing and standardizing lepromin, also the methods adopted in tuberculin testing.

Thereafter, a statistical study is made of the results with the lepromin and tuberculin tests in 81 children and 278 adults, and these are compared with the results of similar experiments made by DHARMENDRA and JAIKARIA in India [this *Bulletin*, 1942, v. 39, 226] and by CHAUSSINAND in Paris. The conclusion is reached that these 3 studies made by different sets of workers, using different methods at different times and in different countries, all point to the same conclusion, that the 2 tests are not independent, and there is some factor operating strongly to make the two tests agree. Four possibilities are discussed as to what this factor may be: exposure to leprous infection, exposure to both infections or to neither, some other acid-fast infection working secretly in the system, or exposure to tuberculous infection making people allergic to the leprosy bacillus. The fourth of these is considered as by far the most likely. "On this basis it is easy to explain how most healthy persons in most countries are allergic to both bacilli or to neither. In West Africa, however, and in countries with much leprosy, it is more than possible that some persons have been exposed to leprous infection but not to tuberculous infection, and this would explain those cases which are lepromin-positive and tuberculin-negative. . . . Analysis of the 38 such cases in our present series shows that nearly all of them are weakly positive to tuberculin, which suggests that the degree of reaction to tuberculin influences the response to lepromin". Further evidence is given to support this view.

Next, an account is given of the results obtained by various workers from vaccination with BCG in changing the lepromin and tuberculin tests in healthy persons. Their findings indicate that BCG vaccine given orally converts lepromin-negatives to lepromin-positives more frequently and more persistently than it causes corresponding tuberculin conversions.

The authors' own experiments with BCG in 65 healthy persons are next described, all of them being tuberculin-negative, and all but 7 being lepromin-negative before receiving BCG. Intradermal injection of 0·1 mgm. was given in each case. Of 65 previously tuberculin-negative, 64 became positive; of 58 previously lepromin-negative, 40 became positive and 14 doubtful; of the 54 who became lepromin-positive or doubtful, all became tuberculin-postive; of the 64 who became tuberculin-positive, 7 were previously lepromin-positive, and of the rest, 40 became lepromin-positive and 14 more became doubtful. While the tuberculin conversions are more numerous, there is evidence that the lepromin conversions are more permanent. The question arises, whether a BCG-induced positive lepromin reaction has the same significance as one induced by leprous infection, that is, does it indicate the presence of immunity to leprosy? So far the direct evidence of this being the case is scanty. FERNANDEZ (*Internat. J. Leprosy*, 1951, v. 19, 474) reports a group of children inoculated with BCG at birth who have lived for several years with their leprous parents and have failed to develop the lepromatous form of the disease. MONTESTRUC and BLACHÉ [this *Bulletin*, 1951, v. 48, 270] report similar results with 3 children in Martinique where the children were vaccinated at birth and revaccinated 4 times. Now at ages of 12, 10 and 9 they are all still healthy. In another group of children who were vaccinated all are healthy, while 4 others who were not vaccinated have all contracted leprosy, 3 being lepromatous cases.

Regarding the use of BCG for prophylaxis of leprosy the following recommendations are made: (a) It must not be used indiscriminately, but generally it should be confined to healthy persons, mainly children, who are unavoidably exposed to leprous infection. (b) In countries where mass BCG vaccination against tuberculosis is being adopted, it may be difficult so to confine its use. In such countries an attempt should be made to

utilize the mass BCG campaign to give evidence of the value of BCG in the prevention of leprosy. (c) All work with BCG in countries with much leprosy should be planned, carried out and recorded in such a way that it can, in the future, give reliable evidence on the value of BCG vaccination in the prevention of leprosy. (d) It should be made clear that BCG vaccination of those exposed to infection does not remove the necessity for taking every possible step to prevent or minimize contact between open cases of leprosy and healthy persons, particularly children.

The second part of this paper deals with studies in persons with leprosy. The two tests were performed in 91 tuberculoid and 275 lepromatous cases. There is not space to record the details here, but it was concluded that these studies " in marked contrast to similar studies in healthy persons, give no evidence of any cross-allergy and possible cross-immunity between the two infections ".

Lastly, 104 lepromatous cases with negative tuberculin and lepromin findings were injected with 0·1 gm. of BCG. After 2 months the tuberculin results were: 88 positive, 10 doubtful and 6 negative. The lepromin tests were 11 positive, 19 with slight late reaction, 15 with slight early reaction only, and 59 with no reaction. In 30 tuberculoid cases, all tuberculin-negative or doubtful, and 28 lepromin-positive, who were similarly vaccinated, the negative tuberculin tests became positive in 17 and doubtful in 5, and the 8 doubtfuls became positive; while the lepromin test showed a considerable rise in the degree of positivity. *Ernest Muir*

Zubiri, Vidal, A. & Mar Moñux, R. Las reacciones con tuberculina (Mantoux) y lepromina (Fernandez y Mitsuda) en sujetos de zona extenta de lepra. [**Reactions with Tuberculin (Mantoux) and Lepromin (Fernandez and Mitsuda) in Subjects Living in an Area where Leprosy is not Endemic**] Reprinted from *Actas Dermo-Sifiliograficas*. Madrid. 1951, June, v. 42, No. 9, 872–82. [19 refs.]

In a zone where leprosy is not endemic, the Mitsuda and Fernandez reactions in 68 patients tested showed respectively 42·64 and 57·35 per cent. positive. The Fernandez reaction was always positive when the tuberculin test was. If only the 1/10,000 titre of tuberculin was taken, the tuberculin and Fernandez reactions corresponded in 72·05 per cent. of cases. The Fernandez and Mitsuda reactions corresponded in 77·94 per cent. of cases. The tuberculin and Mitsuda reactions were in concord in 70·58 per cent. It is concluded that there is a relationship between the Fernandez and tuberculin reactions " which may represent allergy of the individual tested to the genus Mycobacterium (leprosy or tuberculosis) ". *Ernest Muir*

Brand, P. W. **The Reconstruction of the Hand in Leprosy.** *Ann. Roy. College Surgeons of England.* 1952, Dec., v. 11, No. 6, 350–61, 5 figs. [10 refs.] [Also reproduced in *Leprosy Review*, 1953, Apr., v. 24, No. 2, 104–16.]

A description is given of the deformities and the muscles paralysed in the hands in neural leprosy. The author in Vellore, India, has operated upon over 250 claw fingers, and on 45 thumbs that have lost the power of opposition. From this experience he describes the best operations for these two procedures. First the interphalangeal joints have to be mobilized by active exercise, elastic traction and the application of light plaster splints. For claw fingers Bunnell's sublimis transplantation is the operation of

choice for suitable cases, and interphalangeal arthrodesis for the fingers with stiff joints. For restoration of opposition to the thumb the flexor sublimis tendon to the ring finger is transplanted. Details of these operations are given and the results obtained are well illustrated with photographs. Care has to be taken in helping patients towards rehabilitation after recovery of the use of their hands. They should be taught trades which can be performed by means of easily-handled tools, but trades, such as basket-making, which are dependent on the direct use of the hands, are unsuitable. *Ernest Muir*

Argüelles Casals, D. La cortisona en la reacción leprosa. [**Cortisone in Leprosy Reaction**] *Bol. Soc. Cubana de Dermat. y Sifil.* 1953, Mar., v. 10, No. 1, 23–7. [12 refs.]

Report of a case with encouraging results.

Azulay, R. D. **Histopathological Changes due to Sulfone Therapy. Observations of 449 Lepromatous Leprosy Cases.** *Internat. J. Leprosy.* New Orleans. 1952, Oct.–Dec., v. 20, No. 4, Pt. 1, 485–9.

This is a report on the histological findings in biopsies taken from 449 lepromatous patients who had been under treatment for periods of 1 to 3 years. In 233 there was still the lepromatous structure with bacilli, granular but many still rod-shaped. These patients have still to be considered lepromatous and treated as such under the prophylaxis regulations of Brazil. Another group of 105 showed regressive lepromatous infiltration, chiefly simple inflammatory but still with some Virchow cells, but no bacilli; 108 others showed only the simple inflammatory picture, and in 3 cases there were no infiltrative changes of any kind. In none of them was there any sign of transformation to tuberculoid structure. *Ernest Muir*

Brown, J. A. K. **Leprosy Policy in Uganda.** *Leprosy Review.* 1953, Apr., v. 24, No. 2, 98–103.

After describing shortly the geography and population, etc. of Uganda reference is made to the survey of Ross Innes [this *Bulletin*, 1951, v. 48, 643] in which he estimated the number of cases of leprosy in Uganda at 80,000 with an overall average of 1·7 per cent. The author has found great differences in the percentages of cases in different parts of the country, ranging from 1 to 5 per cent. He describes some fallacies that are apt to enter into the collecting of statistics. One of the difficulties is the scattered nature of the population, there being no towns or villages apart from the very few towns which have come into existence through the planting of industries.

The author refers to the Uzuakoli Leprosy Settlement in Southern Nigeria which he pioneered and organized in 1936. " In Uganda the problem is similar, though conditions are different, and whilst its solution will hinge on the effective use of settlements, the problem in the field will require a somewhat modified orientation ". There are 4 broad principles to be followed in the control of leprosy in Uganda which allow of the necessary elasticity in application: (a) Existing settlements are used as far as they are geographically convenient as Primary Residential Centres from which will radiate area schemes. (b) The use of secondary residential centres staffed by ex-patients and supervised by the District Government Medical Officer and the Agricultural and Forestry Officers. Three of these have already been started and a

fourth is under way. (c) There may later be centres formed for smaller areas, or there may be organized and controlled squatting so as to bring patients nearer to treatment centres. (d) Treatment facilities may be created at existing dispensaries or at specially provided outposts when for any reason organized segregation is not practicable. *Ernest Muir*

HELMINTHIASIS

Harwood, P. D. (Chairman, Cttee. on Common Names of Amer. Soc. Parasitologists) *et al.* **A Preliminary List of Common Names for Helminths.** *J. Parasitology.* 1953, June, v. 39, No. 3, 348–51.

Many worms are attracting attention because they are economically important, and although their Latin names are well enough known to scientists, the English names are not well established. The authors give a preliminary list of Latin names to which are linked the English names most widely used for those species. The list is in 4 parts—Nematoda, Cestoda, Trematoda and Acanthocephala, and in each section the Latin generic and specific names are placed in alphabetical order of genera. Thus, *Ascaris lumbricoides* is described as the large roundworm of man; *Onchocerca volvulus* as the blinding filaria; *Strongyloides stercoralis* as the human intestinal threadworm; *Enterobius vermicularis* as the human pinworm; *Diphyllobothrium latum* as the fish tapeworm of man; *Raillietina cesticillus* as the broad-headed tapeworm; and so on.

The difficulties are obvious. Few alternative names are given, and in England, for instance, *E. vermicularis* is the threadworm and *D. latum* the broad tapeworm. Nevertheless, this may prove a useful list; it contains the names of worms which infect animals as well as those which infect man.

Charles Wilcocks

Joseph, F. H. **Concentration of Parasites in Stools.** *South African Med. J.* 1953, June 13, v. 27, No. 24, 506–8.

The author compared the centrifugal sedimentation method (CS) with Faust's zinc sulphate flotation method (ZF) in the examination of 1,500 specimens of stools in Durban. All microscopical examinations were done by himself, and both techniques were applied to identical portions of each specimen: this was achieved by continuing the ZF technique on the deposit remaining after specimens had been taken for examination from the centrifuged sediment. The technique is described in detail.

The results are shown in 4 tables which show that helminth ova of 8 species were found 692 and 293 times respectively by CS and by ZF: in 439 cases, CS only was positive and in 45 ZF only was positive. Thus the findings for sedimentation were about 2·4 times those of flotation and the number of times that CS alone was positive was nearly 10 times that of ZF. The great majority of ova were those of *Trichuris* or *Ascaris*, but it is noted that *S. mansoni* ova were found 10 times by CS and only once by ZF and, furthermore, that they were found by CS alone 8 times and never by ZF alone. In this connexion, the author quotes the claim of Craig and Faust [this *Bulletin*, 1946, v. 43, 506] that the ZF technique is "efficient for the concentration of *S. mansoni* eggs from feces", and adds that his own contrary result "agrees with the experience of many other workers" [but no references to them are given].

Another table shows that 86 times ova were found in direct smears, but in neither of the concentration methods: possible reasons suggested for this are scanty ova, unequal distribution of ova in the faecal mass, disruption of specimens or degeneration of them by overnight refrigeration.

In the first 300 stools, the deposit remaining after zinc flotation was examined and 81 ova of 5 species were found which had not appeared in the scum—this is taken to indicate that in many cases ova fail to rise to the surface of zinc sulphate solution.

In the case of protozoal cysts, the findings by CS and ZF were 241 and 245 respectively: 5 species are listed, and *E. coli* and *Giardia* predominated. There was thus little to choose between the methods, though the ZF, in addition to being slightly superior numerically, has the advantage of being comparatively free from débris, and hence cysts are more readily seen.

The author's final conclusions are that (1) the sedimentation test is far superior to the flotation method for detecting helminth ova in stools; (2) Faust's process, in this series, was not as efficient for this purpose as the originator claims; (3) Faust's process is somewhat better than sedimentation for concentrating protozoal cysts, but both methods are useful; (4) when Faust's technique is used, it should be supplemented by examination of the washed deposit or by the acid sulphate ether method [this *Bulletin*, 1952, v. 49, 1132]. *H. J. O'D. Burke-Gaffney*

Watson, J. M. **Bilharziasis in South Persia.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1953, Jan., v. 47, No. 1, 49–55, 1 map. [20 refs.]

In this paper the author discusses the problem of urinary schistosomiasis in South Persia, which has never been regarded as a serious problem despite its high incidence in the adjacent Euphrates-Tigris basin [this *Bulletin*, 1953, v. 50, 37]. Attention was focused on the problem, however, by a sudden rise in the number of persons reporting for treatment on Abadan Island in the early summer of 1948; later in the summer the number of cases dropped to the usual figure of 1 or 2 per month. A somewhat similar state of affairs had existed in the summer of 1944, and the conclusion was then reached that schistosomiasis was not endemic on the island, infected persons being visitors or immigrants from endemic areas in Iraq or the adjacent Ahwaz area in Persia lying north-east of Abadan on the Qarun River. The author believes that urinary schistosomiasis is probably endemic in the district west of Ahwaz but definite evidence seems to be lacking.

The present-day figure for cases of urinary schistosomiasis in Abadan is low when compared with nearby Basrah city in Iraq where the disease is endemic and where, in 1947, about 2 per cent. of the population of 93,889 were treated. In Abadan in the same year only 0·01 per cent. of the population of 200,000 required treatment. But during recent years the number of cases of urinary schistosomiasis treated by the Anglo-Iranian Oil Company Health Service in south-west Persia has shown a small but steady increase and on Abadan Island during the past 20 years the number has risen from 2 to over 20 cases per annum. The author emphasizes that this may be an apparent rather than a real increase, related among other factors to increased " treatment-mindedness " of the population. Further investigations of an epidemiological nature were deemed desirable, however, and the author carried out a survey of Abadan Island and Ahwaz.

The first part of the investigation consisted of a urine survey. Since numbers of cases treated do not give a true indication of incidence for reasons which are well known, an attempt was made to establish minimum incidence figures for schistosomiasis in both areas by random urine samples

from children and clinic patients. On Abadan Island these samples also included urine from labourers who were engaged in weed-clearance from water-courses. The results of the examination of several hundred smears of urinary sediment proved negative for both areas. The negative results from Abadan were not unexpected since the territory of Iraq, south of Basrah on the other side of the Shatt-al-Arab is known to be free from the disease. The negative results from the Ahwaz area, however, were unexpected since to the west of this area, in the Amarah marshes in Iraq, the disease is heavily endemic and this region is connected with Ahwaz by a continuous belt of marshy ground that becomes drier towards Ahwaz where it is cultivated and contains numerous villages, and there is little doubt that traffic passes from Amarah to Ahwaz. In these villages haematuria is not uncommon but urine samples from the inhabitants were not examined. The author states his opinion that " the facts available point to an extension of the heavily endemic area of the Amarah marshes in Iraq eastwards to the region surrounding the Iranian city of Ahwaz ".

The second part of the investigation consisted of a snail survey of the 2 areas carried out in July, a season when snail populations are maximal. The author believes that it is probable that *Bulinus truncatus* is the vector in South Persia but this snail was not found in either Abadan or Ahwaz. He points out that the environmental conditions on Abadan Island are similar to those on the opposite bank of the Shatt-al-Arab where, despite diligent search, *Bulinus* has never been found. The snail survey of the Ahwaz area which did apparently include the settlements between Ahwaz and the Iraq border was less thorough than that on Abadan Island and the author believes that, as urinary schistosomiasis seems to be endemic in the Ahwaz area, it is likely that *B. truncatus* would be found by a more prolonged and extensive search. The paper ends with suggestions for an explanation of the apparent absence of *B. truncatus* from the waters of Abadan Island. It is suggested that periods of exceptional salinity through tidal action in the rivers which supply all the fresh water on the island limit the effective colonization of otherwise apparently suitable habitats by the molluscs, but this does not explain why such salinity should affect *B. truncatus* more than other kinds of water snails which are easily found there. Such tidal action does not affect Ahwaz. *R. B. Griffiths*

Schadewaldt, H. Die Erstbeschreibung und -abbildung von Bilharzia haematobia und mansoni durch Theodor Bilharz [**The First Descriptions and Illustrations of** *S. haematobium* **and** *S. mansoni* **by Theodor Bilharz**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1953, June, v. 4, No. 3, 410–14, 3 figs. [17 refs.]

The English summary appended to the paper is as follows:—

" Based on personal letters a historical sketch is given of the discovery of *Schistosomum haematobium* and *Schistosomum mansoni* by Theodor Bilharz in Egypt 100 years ago. The original drawings made by Bilharz of male and female worms in copulation, also of typical eggs, are reproduced. The question of name priority—Bilharzia v. Schistosomum—is discussed."

Moore, D. V., Thillet, C. J., Carney, Dorothy M. & Meleney, H. E. **Experimental Infection of** *Bulinus truncatus* **with** *Schistosoma haematobium*. *J. Parasitology*. 1953, Apr., v. 39, No. 2, 215–21. [17 refs.]

This paper begins with a summary of the difficulties which have been experienced in the past in the experimental infection of *Bulinus truncatus*

with *Schistosoma haematobium*. In preliminary observations, the authors used snails which varied from apparently young to fully mature specimens and these were exposed to varied concentrations of miracidia. The results which followed were variable, but snail infections could not be obtained with any degree of regularity.

Since in some trematode infections the susceptibility of the molluscan host to infection is highest in very young specimens, the authors decided to compare the susceptibility of very young *Bulinus truncatus* (1–7 days of age) with older snails of the same species (1½–5 weeks of age). The snails in the very young group were exposed to 5–10 miracidia each, and the snails in the older group were exposed to 10 miracidia each. The results showed that the percentage of snails in each group which survived the incubation period was approximately the same (79·6 per cent. of 398 snails survived in the very young group and 80·2 per cent. of 389 snails in the older group); the age of the snails at the time of exposure had no effect on the length of the incubation period. The significant and important difference between the two groups occurred in the infection rate. In the very young group 50·5 per cent. of the snails surviving the incubation period shed cercariae in contrast with 19·9 per cent. in the older group.

The authors concluded that *Bulinus truncatus* is most susceptible to experimental infection during the first 7 days after hatching and they have now adopted a routine technique which involves the removal of egg masses from the stock aquaria once per week; one week later the newly hatched snails are exposed to infection. They stress that despite this improved technique difficulties in experimental work still exist since, in their experiments, the longevity of the snails which were discharging cercariae did not exceed 21 days. They suggest further study of factors which might lead to increased longevity of discharging snails: the optimum number of miracidia for exposure of the molluscs requires to be determined. *R. B. Griffiths*

Cowan, N. M. **A Case of Urinary Bilharziasis caused by** *S. mansoni* **and** *S. haematobium* **with no Intestinal Involvement.** *J. Roy. Army Med. Corps.* 1953, July, v. 99, No. 4, 185–6.

An African in Kenya, suffering from haematuria, passed a single ovum *S. mansoni* in the urine. Repeated daily examinations were negative for a month, after which ova of both *S. mansoni* and *S. haematobium* were present. Physical and X-ray examinations of the kidney and bladder were negative, but cystoscopy showed the presence of schistosomal nodules around the ureteral orifices and fundus of the bladder. No ova were found in the stool on repeated examination.

The author states that the subsequent presence of *S. haematobium* in the urine in this case confirms the theory that it is demonstrable whenever *S. mansoni* is present in the bladder, even though the *S. haematobium* does not necessarily reveal itself in the urine [Gelfand, this *Bulletin*, 1950, v. 47, 903]. *H. J. O'D. Burke-Gaffney*

Ravisse, P. Sur un cas de bilharziose intestinale à *Schistosoma intercalatum*. [**A Case of Intestinal Schistosomiasis Due to** *Schistosoma intercalatum*] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 327–8.

At Impfondo, in the Middle Congo, an African woman with abdominal pain was found to harbour *Ascaris* eggs and was treated with oil of chenopodium. She returned a week later with the same symptoms and several

large eggs with axial terminal spines were found in the stools. The history and general examination were not significant. No eggs were found in the centrifuged deposit of the urine.

The author discusses briefly the previous records of *Schistosoma intercalatum* and notes that 5 cases were found in the French Congo by CLAPIER in 1920 [this *Bulletin*, 1922, v. 19, 206], but none seems to have been recorded since. The present patient had lived in the area for 8 years, on the opposite bank of the river to that in which the infection had been recorded by Belgian workers. There is thus presumably a small focus in this part of Lower Oubangui, but it is probably not important and unlikely to spread owing to the low density of population. No cases were found by the author in a systematic survey of local schoolchildren.

The question is posed whether the original treatment of the *Ascaris* infection "reactivated" the *S. intercalatum*. [No other details of the eggs are given.] [See also this *Bulletin*, 1953, v. 50, 631, in which a case is claimed in Oubangui-Chari.] *H. J. O'D. Burke-Gaffney*

See also p. 938, ABDINE and YOUSSEF, **Needle Biopsy in the Diagnosis of Liver Disease in Egypt.**

i. GELFAND, M. & ROSS, W. F. **I. The Distribution of Schistosome Ova in the Alimentary Tract in Subjects of Bilharziasis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1953, May, v. 47, No. 3, 215–17.

ii. ———— & ————. **II. The Distribution of Schistosome Ova in the Genito-Urinary Tract in Subjects of Bilharziasis.** *Ibid.*, 218–20. [17 refs.]

i. A systematic search was made for schistosome ova in the alimentary tract and the anatomically related viscera (such as the liver, gall-bladder, pancreas, suprarenals, spleen and mesenteric lymph glands) at autopsies on adult Africans dying in Salisbury, S. Rhodesia, of diseases other than schistosomiasis. The presence of eggs in the organs was determined by digestion of samples of them in 10 per cent. caustic potash for 24 hours at 37°C., and microscopical study of the centrifuged deposit. By this means 110 cases of bilharzial infection were disclosed, and the considerable frequencies of recovery from the various organs of the ova of *Schistosoma mansoni* and *S. haematobium* are set out in a table [which should be consulted in the original]. From a study of this it is evident that the ova of either parasite are not infrequently recovered from the small as well as the large intestine; and that the vermiform appendix commonly (63 per cent.) yields them, though clinical appendicitis is unusual in the African. From all the organs systematically examined, including the liver, *S. haematobium* ova were more frequently recovered than were those of *S. mansoni*. When so many abdominal viscera are likely to be infected in a single person, clinically it becomes difficult to assign abdominal symptoms to involvement of a single viscus or organ.

ii. A detailed study was made of the distribution of schistosome eggs in the genito-urinary tracts of the 110 adult African patients found at autopsy to harbour *Schistosoma haematobium* and *S. mansoni* infections. These were 86 males and 24 females. In all cases the entire bladder and kidneys were removed, in some the ureters, and in some the genitalia and their appendages, for digestion in caustic potash. A pure *S. haematobium* infection was found in at least 68 males and 20 females, and a pure *S. mansoni* infection in at least 39 males and 10 females; there were mixed infections

with both parasites in at least 29 males and at least 8 females [from the figures given the totals are not entirely clear]. The detailed results are set out in two tables [which should be consulted in the original], and they confirm the conclusions already reached as to the prevalence of these parasites among the African population drawn into the Salisbury area. While *S. haematobium* infection, as might be expected, much more commonly involves the prostate than does *S. mansoni*, nevertheless its involvement (57·9 per cent. of males) is not as high as might be expected in view of the prostate's close anatomical relationship to both the bladder and the rectum. The female genital tract is much more commonly involved in *S. haematobium* infection than in *S. mansoni* infection, and local damage to it may result in clinical salpingitis, cervicitis and oöphoritis. [See also this *Bulletin*, 1949, v. 46, 846.] *A. R. D. Adams*

Abbott, P. H. & Spencer, H. **Transverse Myelitis due to Ova of** *Schistosoma mansoni*. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1953, May, v. 47, No. 3, 221–3, 2 figs. on pl. [12 refs.]

Two patients suffering from myelitis, of schistosomal origin, were seen in the Sudan.

The first was an African male aged 35 years who died, and in whom the diagnosis was confirmed at autopsy by recovery of living and of dead *Schistosoma mansoni* eggs from granulomatous areas found in the spinal cord from the level of the 11th thoracic down to and including the 2nd sacral segment.

The second was a young Sudanese male suffering from spastic paraplegia, who was passing *S. mansoni* eggs in the stools. Treatment with antimony tartrate produced marked improvement.

No adult worms were found in the spinal veins of the first patient, but it is suggested that a wandering gravid female was present in the adjacent extramedullary spinal veins, or adjacent vertebral venous plexus. Free venous anastomosis between the pelvic veins and the vertebral venous plexuses has been demonstrated; this in conjunction with the anastomoses between the systemic pelvic veins and haemorrhoidal portal veins would provide a route of travel for the migration of a gravid worm from its normal habitat. The ova deposited by it, by partially blocking the intramedullary spinal veins, would obstruct the venous return and produce small venous infarcts in the cord, and the ova themselves would excite a granulomatous reaction. The improvement following treatment in the second case was probably due to the withdrawal of the causative worm, as a result of the action of the drug, with relief of the venous congestion in the adjacent cord.

As paraplegia is not infrequent in the Sudan, where both the commoner schistosomal parasites are prevalent, it may well prove that infection with these is the cause of it more frequently than has been suspected. [See also this *Bulletin*, 1950, v. 47, 903.] *A. R. D. Adams*

Belhommet, F. Essai de thérapeutique de la bilharziose par la Carbilazine. [**Trial of Carbilazine in the Treatment of Schistosomiasis**] *Ann. Soc. Belge de Méd. Trop.* 1953, Feb. 28, v. 33, No. 1, 3–11.

Carbilazine is described as "le citrate de Diaethyl-carbamyl-méthyl-pipérazine" [diethylcarbamazine, hetrazan]. It is put up in tablets each containing 50 mgm. of the drug. It was given to 24 adult Africans suffering from schistosomiasis [species not stated, but the ova were found in the

stools] who had not previously been treated specifically for the infection. The dosage initially was 3 tablets twice daily, and later was 5 to 8 tablets twice daily according to the weight of the patient. The duration of a course of treatment was from a week to 10 days; the number of tablets taken during each course ranged from 50 to 140. The course was repeated in some of the earlier cases, initially given a small total dosage, on 1 or 2 occasions after an interval of 1 to 3 or 4 weeks. When later it became clear that a greater total dosage could be given with impunity this was no longer necessary. There were no toxic side-effects of consequence attributable to the drug, but about one-third of the patients suffered from a pruritus over the lower abdomen, pubis and groins. This was ascribed to the destructive action of the drug on the parasites, and was readily controlled by giving an anthistaminic.

The immediate effect of the treatment appeared to be good in that eggs almost or entirely vanished from the stools in every case. Ten of the patients were re-examined 9 to 18 months later; 6 of them appeared still to be free from the infection as no eggs were found in their stools.

A. R. D. Adams

Tomberg, V. & Lagrange, E. Étude de l'action de quelques agents physiques sur les Planorbes et les Cercaires de *Bilharzia mansoni*. [**Study of the Action of some Physical Agents on Planorbids and on the Cercariae of** *S. mansoni*] *Ann. Soc. Belge de Méd. Trop.* 1952, Oct. 31, v. 32, No. 5, 501–11, 3 figs.

The authors' summary in French is translated freely as follows:

The destructive effects of supersonics, ultra-violet rays and short-wave electric fields were studied in relation to cercariae and planorbid snails, by means of different commercial and laboratory-made apparatus, having in mind their application in the field.

The destructive effect depends on the integral dose (intensity × time) applied. We have therefore paid particular attention to the exact measurement of the dose, so as to be able to assess the minimum required for sterilization under practical conditions with the apparatus employed.

The short- and ultra-short waves have the widest field of effectiveness but their destructive effects depend on a specific thermal action.

The supersonics have a less effective range of action but have the advantage of producing two destructive effects, namely, a specific thermal action and a mechanical (and chemical) action by "*cavitation*".

The effective range of ultra-violet rays is the most limited of the 3 methods studied. They act by the actinic effect of the bactericidal spectral rays (primary and secondary) in the region of 2,540 Å. The radiation intensity of these rays is quickly attenuated by water and the action in depth, as expressed by half-value thickness of absorption ["*mi-valeur d'absorption*"] is in the region of 15 to 25 cm. for pure water and 20 cm. for swimming pool water.

To compare the technical results of these 3 methods one must take into account the volume of water to be sterilized per hour and the depth of action required. This being fixed, for an average swimming pool one can calculate the necessary strength of the emitting apparatus. Our calculations generally showed that sterilization is actually practicable by the appropriate methods, from the financial aspect, especially for swimming pools and still waters.

J. J. C. Buckley

Knönagel, H. Über einen Fall von menschlicher Infektion mit dem Katzenleberegel *Opisthorchis felineus* (Riv.). [**A Case of Human Infection by** *Opisthorchis felineus*] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1953, June, v. 4, No. 3, 389–94, 2 figs. [14 refs.]

The English summary appended to the paper is as follows:—

"Eggs of *Opisthorchis felineus* (Riv.) were found in liver tissue sections of a jaundiced patient in a Berlin hospital. The infection had probably taken place in Crimea 10 years before. While repeated treatment with resochin and fuadin improved the patient's general condition, Opisthorchis eggs still showed in the duodenal juice one year later."

Wigand, R. & Warnecke, W. Benzinum Petrolii (DAB 6) in der Therapie der Taeniasis (*T. saginata*). [**The Treatment of Taeniasis** (*Taenia saginata*) **with Benzine (DAB 6)**] *Med. Klin.* 1953, July 3, v. 48, No. 27, 964–5.

The authors refer briefly to earlier work on the use of benzine as an anthelmintic. It is used by the people of Northern Anatolia for this purpose and Biyal [this *Bulletin*, 1948, v. 45, 802] tried it.

The authors treated with it 20 patients all infected with *Taenia saginata* only. The treatment of 17 of these patients was successful and that of 3 was not. Biyal [*loc. cit.*] obtained 48 cures with no result in 4 cases, but he does not state the species of parasite treated. In the authors' cases scolices were found in the stools in only 5 cases, but they attribute this to the fact that the benzine has a solvent action on the tapeworm, proglottides passed being in a state of partial solution. The treatment was in part combined with insufflation of oxygen into the duodenum, a method which Wigand has studied. Two-thirds of the patients had had more than 2 previous treatments. Because the prospect of cure is less favourable when previous treatments have been given, the authors think that their results must be reckoned better than those that would have been obtained with patients having their first or second treatments.

The patients were prepared by a previous evacuation with Carlsbad salts or infusion of senna, magnesium sulphate being avoided, because it may cause somnolence and other toxic effects. The benzine is given as an emulsion in gum arabic, the prescription for which, based on that of Biyal [*loc. cit.*] is given. The preparation used was "Benzinum petrolii (DAB 6)", which is presumably a petrol-like substance. The dose contained in the emulsion was 60 cc. for adults, 20 cc. for children of 2 to 5 years and 30 cc. for children from 6 to 14. It may be taken fasting by the mouth, when it may cause nausea and rarely vomiting or other gastric troubles. The authors recommend that it should be given directly into the duodenum under the control of a sound, the head of which lies in the descending limb of the duodenum. The gum arabic lessens the local action of the benzine, which may cause desquamation of duodenal epithelium or more severe gastric or intestinal troubles, but the authors found no blood in the stools. Abdominal diseases contra-indicate the treatment. Because the drug is inflammable, its use should be restricted to clinics. [In the abstract of Biyal's paper cited above, the substance is erroneously referred to as "benzene": the dose of benzene (benzol) is, of course, 5 to 10 minims. In any case, 60 cc. of benzine seems heroic.] *G. Lapage*

Garcia, M. F., de Mattos, A. & Bürger, H. A acção tenífuga do ácido diiodofenilpropiónico. [**Diiodophenyl propionic acid in the Treatment of Taeniasis**] *Gaz. Méd. Portuguesa.* 1953, v. 6, No. 2, 355–9. English summary.

The more formidable, fuller name of this drug is β(4-hydroxy-3,5-diiodophenyl) α-phenyl propionic acid or β-phenyl-β carboxyl-(3,5-diiodo-4-hydroxyl phenyl) ethane. Its use is advocated for various forms of cestode infestation, *Taenia saginata*, *T. solium*, *Diphyllobothrium latum*, *Hymenolepis nana* and *Dipylidium caninum*. It is taken by mouth as tablets, each of 0·5 gm.; no special preparation is needed, dietetic or otherwise, it produces no untoward symptoms and is well tolerated. Three grades of treatment may be adopted. By the first, 6 tablets are given at 5-minute intervals, after dinner or at bedtime. If the worm and scolex are not eliminated the following day, the "double dose" method is undertaken after an interval of 2 or 3 days. By this, 12 tablets (6 gm.) are given, 2 each at 5-minute intervals, followed next morning by a saline purgative. If this also is unsuccessful, after a fortnight the "triple dose" method is practised: 6 tablets after early morning coffee, 6 at about noon and 6 after dinner, also followed next morning by a purge. [The authors call this "12 grs." throughout, but if the tablets are of the same size and strength, the total would be 9 gm.] For children under 12 years of age, the first course of 6 tablets is given, but no purgative.

The authors speak in detail of 15 patients, 13 with *T. saginata* and 2 with *T. solium*. All had had other treatments ineffectually; their ages ranged between 14 and 65 years; 12 were males, 3 were females; 6 were Portuguese, 5 were Brazilians, 2 Germans, 1 Italian and 1 Pole. All had passed ova or proglottides and were showing the usual symptoms of nausea, abdominal pain or discomfort, flatulence, loss of weight, urticaria, diarrhoea and subjective disturbances; 9 had eosinophilia of 7 to 18 per cent. and 5 were anaemic; one had also *Ancylostoma duodenale* infection. Ten of the 15 were given the "triple dose" without saline purge, the other 5 had the purgative also. Of the former, 8 expelled the worm and scolex, 2 the worm but no scolex; of the latter 4 expelled the worm and scolex, the fifth no scolex. After 15 days' interval the "triple dose and purgative" was given to these 3 and only one failed to pass the scolex. Since the drug is well tolerated and easy to administer, it is worthy of more extensive trial.

H. Harold Scott

Čmelik, S. & Briski, B. Untersuchungen über Eiweissfraktionen von *Taenia echinococcus*. [**Studies of the Protein Fraction of** *Echinococcus granulosus*] *Biochem. Ztschr.* 1953, v. 324, No. 2, 104–14, 3 figs. [31 refs.]

Ackert, J. E. **Some Influences of the American Hookworm.** Reprinted from *Amer. Midland Naturalist.* 1952, May, v. 47, No. 3, 749–62, 4 figs. [19 refs.]

The hookworm is responsible for much that is evil, but the author here traces its indirect influence for good. It is largely the story of the activities of 3 men; Stiles, who recognized the importance of *Ancylostoma duodenale*, described *Necator americanus* and devoted his life to hookworm campaigns; Page, an enlightened and adventurous journalist who took much interest in Stiles's work, and Gates, of the Rockefeller Sanitary Commission.

Stiles's and Page's propaganda led to the formation of the Rockefeller Sanitary Commission for the Eradication of Hookworm Disease, and

through this to the creation of the Rockefeller Foundation and its International Health Division. Johns Hopkins School of Hygiene was created to train staff for the Foundation's work. International cooperation, especially the principle of the demonstration team combined with fellowships, arose from hookworm campaigns, to which the origin of Peiping Union Medical College was also largely due. Lastly, the combination of destruction of cotton crops in the southern U.S.A. by boll weevil, with debilitation of plantation workers by hookworm disease, led to the formation of a combined agricultural and health policy which revivified the South. *G. Macdonald*

Üner, R. Askaridozda kütireaksiyonundan alinan neticeler. [**Cutireaction to Ascarides**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi.* Ankara. 1952, v. 12, No. 2, 119–24. [13 refs.] [Summary taken from *J. Amer. Med. Ass.* 1953, May 16, v. 152, No. 3, 265.]

In rural communities of Turkey helminthiasis is present in 80% of the population. Prof. Ziya Oktem, of Istanbul University department of microbiology and infectious diseases, when chief of the Black Sea coast Necator campaign, found ascarides in 55% of the inhabitants of this region. Dr. Kadri Onat found ascarides in 38% of the inmates of the Istanbul Asylum for the Aged Poor. Dr. Ragip Üner found ascarides in all the pupils of a primary school in Newshehir, a town in central Anatolia.

In the *Turkish Bulletin of Hygiene and Experimental Biology* (vol. 12, no. 2, 1952), Prof. Nusret Karasu, of the department of phthisiology of Ankara University, and his associate, Dr. Ragip Üner, have published their results with experiments of ascarides extract. Ascarides were exposed to a high pressure flow of running water, hacked into minute pieces, and crushed with sterile sand and physiological serum in a sterile mortar. The solution obtained was sterilized in formalin and put into ampules, which were kept in a refrigerator. From 80 ascarides 20 to 30 cc. of extract was obtained, and from this the desired solution was taken. Separate extracts were prepared from female ascarides and their eggs and from male ascarides. As far as the tests were concerned, no difference was observed. The first administration evoked a histamin-like shock in the patient. A further diluted solution did not have that effect. Currently a tenth of a 1:8,000 solution is accepted as a unit. A subcutaneous injection of 1 unit produces a 10 mm. erythema, in the centre of which an edema develops; it disappears after 48 hours. For control a subcutaneous injection of a salt solution was given in the other arm. The cutireaction test was administered to 941 persons 1 to 60 years of age. Seventy-five per cent of those who expelled ascarides or whose feces revealed their eggs had positive reactions; 18% who did not expel ascarides and whose feces did not reveal eggs had positive reactions. When other parasites were also present the tests were 100% positive. In hospital patients with tuberculosis the reactions were 89% positive, in patients with ulcers 70%, and in patients with lymphogranulomatosis, asthma, and cirrhosis positive reactions were negligible. In children up to 5 years old positive reactions were 69%, in patients from 5 to 20 years old 60%, and in those from 20 to 30 years 65%.

Bueding, E. **Formation of Tiglic and *n*-Valeric Acids by Bacteria-Free *Ascaris lumbricoides*.** *J. Biol. Chem.* 1953, June, v. 202, No. 2, 505–12, 4 figs. [17 refs.]

"The isolation and identification of *n*-valeric and tiglic acids as metabolic products of bacteria-free *Ascaris* are reported."

Bevacqua, R. Infestations provoquées par les helminthes chez les enfants d'une école primaire de Milan. [**Helminth Infections in Primary School Children in Milan**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 406–11.

The author examined stools of 538 schoolchildren in Milan, chiefly by Willis's technique. The results are set out in 7 tables together with statistical analysis of them.

The chief points of interest were that helminths were found in 28·12 per cent. of children, that *Trichuris* (20·4 per cent.) was the commonest and *Ascaris* (7·8 per cent.) next: *Trichuris* affected chiefly boys, and infection seemed to be independent of age. *Ascaris* affected both sexes equally, and the numbers of children harbouring it decreased with age from 6 to 11 years.

H. J. O'D. Burke-Gaffney

Saggese, S. Osservazioni epidemiologiche sui casi di echinococcosi operati a Roma dal 1941 al 1951. [**Epidemiological Studies on Echinococcal Infections in Patients Treated Surgically in Rome from 1941 to 1951**] *Nuovi Ann. d'Igiene e Microbiol.* 1953, Jan.–Feb., v. 4, No. 1, 45–52, 4 charts.

The English summary appended to the paper is as follows:—

"The most important result of an epidemiological nature drawn from a statistical investigation made on 1,070 patients who underwent surgical treatment for hydatidosis, in the hospitals and University Clinics of Rome from 1941 to 1951, are reported. The collected data show clearly the progressive increase of echinococcosis in these last ten years among adults, as well as among children. The disease is more frequent in males (590) than in females (480). Although the largest incidence is encountered in farmers, nevertheless all groups of wagearners have been affected. A third of the cases came from Rome and its province; the others from almost all provinces of Italy.

"In the clinical histories the presence or contact of dogs in patients' homes are shown as occurring only in 10 per cent of the cases. One may therefore suppose that the disease can perhaps be transmitted through contaminated food.

"Attention is drawn upon the very high rate (60 per cent.) of pulmonary localisations, which is the highest rate reported to date for the entire world."

Kushlan, S. D. **Trichinosis with Liver Dysfunction, Hypoalbuminemia, and Typhoid Agglutinins.** *J. Amer. Med. Ass.* 1953, May 16, v. 152, No. 3, 221–4, 2 figs.

Trichinosis is one of the most common and important parasitic diseases of the United States. Digestion of diaphragms obtained at post-mortem examination in one survey has shown 37 per cent. of them to be infected with the cysts of *Trichinella spiralis*. The clinical diagnosis of trichinosis may be difficult, and there is no specific treatment for the condition, though corticotropin (ACTH) or cortisone may relieve symptoms and lessen tissue damage. The prognosis depends on the locality of the encysted larvae and their numbers; the average mortality in different outbreaks has been 10 per cent.

Full details are given at some length of the occurrence of acute trichinosis in a white male aged 62 years, who survived the infection. The diagnosis was established by muscle biopsy. There were physical and X-ray changes in the lungs, electrocardiographic changes, and some enlargement of the liver with abnormal cephalin and thymol flocculations and thymol turbidity, in addition to the usual evidence of involvement of the skeletal musculature and the gastro-intestinal tract. There was a substantial eosinophilia; the serum albumin was reduced; and although the Widal test initially had been negative, it became positive to both typhoid H and typhoid O in rising titre within 3 weeks of the patient's admission, while no evidence of a typhoid infection was found. *A. R. D. Adams*

Zaiman, H. **Studies on the Nature of Immunity to *Trichinella spiralis* in Parabiotic Rats. I. A Preliminary Study of the Immune Response of the " Uninfected " Rat as determined by Observation of the Intestinal Phase.** *Amer. J. Hyg.* 1953, May, v. 57, No. 3, 297–305. [35 refs.]

" Infection of one member of a pair of parabiotic rats with a known number of *Trichinella spiralis* larvae in a single dose usually made that rat resistant to reinfection 1 month later. The resistance of the ' uninfected ' twin was considerably greater than that of rats in control pairs but less than that of its infected mate."

Zaiman, H., Omi, G. & Gapinski, L. **Studies on the Nature of Immunity to *Trichinella spiralis* in Parabiotic Rats. II. A Preliminary Study of the Immune Response of the " Uninfected " Rat as determined by Observations of Muscular Invasion.** *Amer. J. Hyg.* 1953, May, v. 57, No. 3, 306–10.

" More evidence was offered to confirm a previous conclusion that when one member of a pair of parabiotic rats is infected with a single dose of *Trichinella spiralis* larvae, the resistance of its ' uninfected ' twin was considerably greater than that of rats in control pairs."

Zaiman, H. & Rubel, June. **Studies on the Nature of Immunity to *Trichinella spiralis* in Parabiotic Rats. III. The Immune Response in Parabiotic Rats surgically separated from their Mates Five Days after One Member of the Experimental Pairs received an Immunizing Dose of *Trichinella spiralis*.** *Amer. J. Hyg.* 1953, May, v. 57, No. 3, 311–15.

" Three small experiments are reported in which parabiotic rats were surgically separated from their mates 5 days after one member of each experimental pair was infected with *Trichinella spiralis* (15 larvae per gram of body weight). One month after the infected rats received the immunizing infection, all rats were given a challenge dose of 5 larvae per gram of body weight. In each experiment the ' uninfected ' member of the experimental pairs was more resistant to the challenge infection than were the controls."

DEFICIENCY DISEASES

Sillans, R. Sur quelques plantes alimentaires spontanées de l'Afrique Centrale. [**Some Edible Plants of Central Africa**] *Bull. Inst. d'Études Centrafricaines.* (n.s.) 1953, No. 5, 77–99. [Numerous refs.]

Bothwell, T. H., van Doorn-Wittkampf, H. van W., Du Preez, M. L. & Alper, T. **The Absorption of Iron. Radioiron Studies in Idiopathic Hemochromatosis, Malnutritional Cytosiderosis, and Transfusional Hemosiderosis.** *J. Lab. & Clin. Med.* 1953, June, v. 41, No. 6, 836–48, 2 figs. [34 refs.]

A standard dose of 20 mgm. of iron labelled with radioiron was given by mouth to 5 patients with idiopathic haemochromatosis, 5 patients (South African negroes) with malnutritional cytosiderosis, 3 patients with transfusional haemosiderosis and 8 control subjects. All were on routine hospital diets. The proportion of the dose detectable in the blood and the proportion excreted in the faeces (except in the cases of malnutrition) were measured, as also measurements of the *gamma* rays recorded by a counter over the liver and other organs.

Over 75 per cent. of the dose was recovered in the faeces in all cases examined except one of idiopathic haematochromatosis, from whom only 28 per cent. was recovered. From 2 other patients with this condition high recoveries were obtained with a first test dose, but only 23 per cent. and 65 per cent. of second doses. Over 3 per cent. of the test dose was detected in the blood in 3 out of 8 tests on the patients with idiopathic haematochromatosis, all but one of whom gave high liver counts. In none of the malnutritional cytosiderosis patients, in only one of the transfusional haemosiderosis and in 3 out of 8 controls did the blood ever contain over 3 per cent. of the total dose. In these 3 groups only, one patient with malnutritional cytosiderosis gave appreciable counts over the liver. [These figures taken from an excellent table show clearly the excess storage of iron in the liver of patients with idiopathic haematochromatosis and the variations in absorption of iron in all groups. These are so great that many more patients would have to be studied before general conclusions could be drawn.]

R. Passmore

Govindan, K. K. & Radhakrishna Rao, M. V. **Studies on Lipotropic Factors. Part I. Choline Content of the Serum in Normal and in Patients suffering from Cirrhosis of the Liver.** *Indian J. Med. Res.* 1952, Oct., v. 40, No. 4, 505–10. [20 refs.]

"1. The choline content of the serum in 17 normals, 7 cases of infantile cirrhosis, 31 cases of adult cirrhosis and 15 displaced persons suffering from anaemia and undernutrition is reported.

"2. The results do not show any difference in the choline content between normals and patients with liver disease. The slightly lower choline content of serum of displaced persons is probably due to their generally lower standard of nutrition.

"3. The results do not suggest that choline content of the serum will be of value in the diagnosis or prognosis of liver cirrhosis."

SPRUE

ZUMOFF, B. **Possible Relationship of Folic Acid to Uric Acid Metabolism as exemplified by a Case of Non-Tropical Sprue.** *Amer. J. Med. Sci.* 1953, June, v. 225, No. 6, 674–6, 2 figs.

"A case of non-tropical sprue with megaloblastic anemia is described, in which it is noted that a high blood uric acid level was present during relapse. Following successful treatment of the anemia with folic acid, the blood uric acid level was observed to decrease markedly. Possible explanations for this are discussed, and theoretical and experimental evidence is cited to support the hypothesis that hyperuricemia may sometimes be a chemical sign of folic acid deficiency."

DE LANGEN, C. D. De bloeddruk bij patiënten met steatorrhoe. [**The Blood Pressure in Patients with Steatorrhoea**] *Nederl. Tijdschr. v. Geneesk.* 1953, July 11, v. 97 (iii), No. 28, 1830–31.

The English summary appended to the paper is as follows:—

"After the publication of SALVESEN about the occurrence of hypotension as a regular symptom with steatorrhoea the author made an analysis of his own cases of sprue. But his material was different. The greatest part of his patients was suffering from tropical sprue, while Salvesen did not mention one case of tropical origin. The author confirmed the fact to which Salvesen pointed, that all these patients had a low, some of them a very low blood tension. The explanation of this phenomenon is not easy. Salvesen thinks that most probably there is also a disturbance in the absorption of a substance (probably a lipoid) which is necessary for maintaining an adequate blood tension. The author proposes that the hypotension is not the result of the steatorrhoea, but on the contrary believes that the syndrome of sprue may develop under influence of an insufficient circulation in the intestinal wall."

HAEMATOLOGY

SUNDERMAN, F. W., MACFATE, R. P., MACFADYEN, D. A., STEVENSON, G. F. & COPELAND, B. E. **Symposium on Clinical Hemoglobinometry.** *Amer. J. Clin. Path.* 1953, June, v. 23, No. 6, 519–98, 16 figs. [469 refs.]

CHALMERS, J. N. M., IKIN, Elizabeth W. & MOURANT, A. E. **A Study of Two Unusual Blood-Group Antigens in West Africans.** *Brit. Med. J.* 1953, July 25, 175–7, 1 diagram.

"An investigation has been carried out into the distribution in West Africa and the genetics of the Hunter antigen of Landsteiner, Strutton, and Chase (1934) and of the newly discovered Henshaw antigen. The genes for both of these antigens appear to be closely linked to those of the MNSs blood-group system."

BJÖRKENHEIM, G. **Influence of Folic Acid on the Nervous System in Pernicious Anemia. Experiences relating to Pernicious Tapeworm Anemia.** *Acta Med. Scandinavica.* 1953, June 23, v. 145, No. 6, 406–9. [17 refs.]

"A case of pernicious tapeworm anemia is described where folic acid therapy during remission resulted in a neurological relapse. The deleterious

influence of folic acid on the nervous system even in cases where the supply of neurotropic factors seems to be optimal is emphasized, and the use of folic acid in combination with liver preparations in the treatment of pernicious anemia is condemned. The causes of the deleterious effect of folic acid and of the development of neuro-degeneration in pernicious anemia are discussed."

YONIS, Z. & SHMUELI, D. [**Mediterranean Anemia (Cooley's Anemia in a Jewish Family in Israel**)] *Dapim Refuiim.* Tel-Aviv. 1953, May, v. 12, No. 1 [in Hebrew 49–54, 6 figs. on 2 pls. & 1 chart. (25 refs.) English summary v].

HOWELL, J. & WYATT, J. P. **Development of Pigmentary Cirrhosis in Cooley's Anemia.** *Arch. Pathology.* 1953, May, v. 55, No. 5, 423–31, 2 figs. [Refs. in footnotes.]

" The characteristic accumulation of iron in Cooley's anemia is emphasized, as this visceral distribution of pigment simulates that observed in idiopathic hemochromatosis. With the advent of multiple transfusions as a therapeutic measure in Cooley's anemia, the complete picture of classical hemochromatosis with the pathologic alterations of pigmentary cirrhosis and pigmentation of the skin, myocardium, and pancreas has been recorded.

" From chemical, morphological, and temporal studies, it is suggested that the development of these distinctive pigmentary lesions with fibrosis is due to continuing or episodic tissue hypoxia, rather than excessive iron storage accumulating from multiple blood transfusions."

VENOMS AND ANTIVENENES

VILLIERS, A. La collection de Serpents de l'IFAN (Acquisitions 1952). [**The Snake Collection of the Institut Français d'Afrique Noire. New Acquisitions in 1952**] *Bull. Inst. Français d'Afrique Noire.* 1953, July, v. 15, No. 3, 1103–27, 5 figs.

JOHNSON, Monica, KAYE, M. A. G., HEMS, R. & KREBS, H. A. **Enzymic Hydrolysis of Adenosine Phosphates by Cobra Venom.** *Biochem. J.* 1953, July, v. 54, No. 4, 625–9, 1 fig. [21 refs.]

LEPESME, P. & DOUCET, J. Sur un cas d'envenimation par *Atractaspis*, vipéridé Ouest-Africain. [**A case of Poisoning by the West African Viperine,** *Atractaspis*] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 2, 207–11, 2 figs. on pl.

Atractaspis bite is regarded by many as non-toxic and by others as relatively harmless and never fatal. Incidentally, the authors object to the term " snake-bite ", because the fangs inject their poison by a prick as of a needle [but a bite is a bite even if the top teeth only penetrate]. The case here recorded is that of a man scratched, not actually bitten, on the tip of the right index finger by a small *Bitis lachesis* (*arietans*). Pain was severe for a few minutes, then ceased and no general symptoms followed, so he continued his occupation.

A quarter of an hour later he came across a small snake, *Atractaspis irregularis*, in some mould he was clearing away; in trying to capture it he was bitten [the author calls it " pricked "] on the tip of the right forefinger and then on the left. Local numbness came on almost at once and extended over the hand, without systemic disturbance. The numbness spread up the arms and the axillary lymph glands were swollen. In 2 hours dyspnoea and tachycardia were present. Two hours after being bitten he was given 10 cc. of antivenin [not specified but stated as A.O.] and in less than an hour he took to his bed. An hour later a second injection was given and he took a large cup of strong coffee. There was no benefit and his temperature was rising (in Viperine poisoning it usually falls) and 4½ hours after infliction of the injury he was taken to hospital. By that time he was mentally dull; pulse 120, temperature 40·5°C., both index fingers swollen and each presented a necrotic patch the size of a 50-centime piece. A third injection was given together with an injection of camphor-sparteine and of penicillin; he was also given nivaquine [chloroquine] as he was a malarious subject. For the next 2 days the temperature remained elevated, 38–40°C. and he was given 2 more injections of antivenin and 300,000 units of penicillin. The temperature did not come down to normal until a week had passed.

Against medical advice he then left to attend a congress at Fernando Po, from the 5th to the 12th December. On his return 2 days later the necrotic foci had not yet completely cleared up and 13 days later still, although cicatrization had begun, there was still a small fistula. With radium therapy healing took place, but a small scar, about 1 cm. in diameter, was present 10 months after the accident. [What part, if any, was played by the poison of the initial wound by *Bitis lachesis* is not referred to.] *H. Harold Scott*

Maretić, Z. **Arachnidism treated with Cortisone.** Report of a Case. *J. Amer. Med. Ass.* 1953, June 13, v. 152, No. 7, 609.

Bites by *Latrodectus tredecimguttatus* may give rise to very serious symptoms: severe and widely distributed pain, tachypnoea, salivation, vomiting and profuse perspiration, convulsions, exaggerated tendon reflexes, flushing, conjunctivitis, oliguria, leucocytosis with reduction of eosinophiles and lymphocytes. In Yugoslavia biting by this spider is relatively common; 101 patients were treated at the General Hospital, Pula, in the years 1948–52.

Details are reported of a man, 52 years of age, bitten during his sleep. He woke with intense pain in the right knee, spreading over the abdomen, chest and back, with burning sensations in the feet. He sweated profusely and vomited, with marked salivation. Respirations were 30 per minute, temperature 36·7°C., pulse 84, face flushed, conjunctivae injected, some oedema of eyelids; the mark of the bite was seen on the mesial side of the right knee. Blood examination showed leucocytes 12,400, eosinophiles 56 per cmm.; " slight neutrophilia and lymphopenia ". Cortone (cortisone acetate) 80 mgm. was injected intramuscularly and improvement set in within 20 minutes. He was less restless and the breathing easier. The pain was less and had almost gone in an hour; improvement continued without interruption. The author thinks that a larger dose might have been given or it might be repeated in severe cases, possibly combined with calcium gluconate or antivenin. *H. Harold Scott*

Lemaire, R., Camain, P., Postel, R., Leduc, Y. & Ehrhard, S. Les effets toxiques des extraits de *Physalia pelagica*. (Note préliminaire.) [**Preliminary Note on the Toxic Effects of Extracts of** *Physalia pelagica*] *Bull. Inst. Français d'Afrique Noire*. 1953, July, v. 15, No. 3, 1128–37, 4 figs.

The following is a translation of the author's summary:

These experiments justify the conclusion that extracts of *Physalia* [the jelly-fish known as "Portuguese man-of-war"] have a toxic action which varies with the animals to which they are administered. The toxic effects take the form of nervous, circulatory, digestive and secretory manifestations, which predominate each according to the species used.

Studies are being continued with the aim of elucidating the mechanism of this toxic action, which is complex. In fact, apart from their toxicity, extracts of *Physalia* have an anaphylactic power. This does not justify identifying the effects of *Physalia* toxin with those of histamine, even though the circulatory, broncho-motor and secretory actions of the two substances appear to be identical. Nevertheless, previous administration of a synthetic antihistaminic (3277RP) suppresses the hypotension which follows the injection of *Physalia* extract in chloralized dogs.

H. J. O'D. Burke-Gaffney

DERMATOLOGY AND FUNGUS DISEASES

Shelley, W. B. **Miliaria.** *J. Amer. Med. Ass.* 1953, June 20, v. 152, No. 8, 670–73, 5 figs.

The term "miliaria" is used for all skin changes resulting from sweat retention. It may be divided into 4 main groups:—

Miliaria crystallina is a superficial, transient rash causing little discomfort. The lesions consist of translucent vesicles filled with sweat.

Miliaria rubra, or prickly heat, is a pruritic, inflammatory papulo-vesicular dermatitis. It occurs as a primary disorder or as a secondary complication of other dermatoses and is probably the commonest skin disease to be found in warm countries. Rapid appearance or disappearance of the lesions in association with elevation or reduction in body or environmental temperature is a characteristic of the disease. The affected areas show either hyperhidrosis or a normal sweat response with 90 per cent. of the glands functioning normally. Symptoms result from the comparatively small number of occluded glands. The sites of predilection are the ante-cubital and popliteal fossae, the chest and the abdomen, the palms and soles being spared.

Miliaria pustulosa occurs as a complication of numerous skin diseases and causes numerous pustules unassociated with hair follicles. Pruritus is severe and associated with sweating. The purulent material is white and usually sterile although occasionally secondary invasion by *Staphylococcus aureus* may occur.

Miliaria profunda is the skin change associated with tropical anhidrotic asthenia. The affected skin is studded with numerous non-inflammatory papules which increase in size when vigorous sweating occurs.

Histologically all 4 conditions can be seen to result from obstruction of a sweat duct. In miliaria crystallina the trapped sweat remains beneath the horny layer; in miliaria rubra and pustulosa it collects in the epidermis, and in miliaria profunda within the dermis proper.

Treatment consists in reducing sweating by means of an air conditioner, electric fans, or any other measures designed to improve ventilation and reduce humidity. Too frequent bathing, excessive use of soap or detergents and irritating topical medicaments should be avoided. Local applications are of no specific value in this condition. *H. T. H. Wilson*

Polunin, I. **Tinea Imbricata in Malaya.** *Brit. J. Dermat.* 1952, Oct., v. 64, No. 10, 378–84, 7 figs.

Tinea imbricata is common in each of the 3 main types of Malayan aborigines and is widely distributed through the Malay Peninsula; 9·1 per cent. of 581 aborigines were found to be affected, no sex or age group being specially susceptible to the disease.

The rash consists of concentric circles of desquamating skin, the scales being adherent peripherally. Within each ring of scales there is a circle of hypopigmented skin and within this a circle of normal skin. This concentric appearance, clearly shown in 7 photographs illustrating the article, is often obscured by scratching and lichenification of the lesions. The prominent parts of the body are principally affected, the groins, parts of the axilla and the front of the scalp being normally spared. The concentric pattern is poorly shown on the face, lips, nipples and axillae where the delicate scales are often removed to leave hypopigmented patches. *H. T. H. Wilson*

Sharvill, D. **Tinea Imbricata in a European: Double Infection with *Trichophyton concentricum* and *Trichophyton rubrum*.** *Brit. J. Dermat.* 1952, Oct., v. 64, No. 10, 373–7, 2 figs.

The case is described of a European police officer aged 23 who contracted tinea imbricata in Malaya and was sent home to England on leave. His eruption was easily diagnosable although not so spectacular as textbook illustrations of the disease.

The hair and nails were unaffected.

For culture half the scales were placed for 5 minutes in alcohol as often recommended, but these remained sterile. The remainder were cultured directly. *Trichophyton rubrum* was grown on 2 tubes of Sabouraud's medium and one of malt extract agar at 22°C. *Trichophyton concentricum* failed to grow on solid media, but grew in one tube of broth at 22°C. and two at 37°C. The resultant colonies are described in detail.

The patient was treated with Whitfield's ointment and the following lotion:— acid salicylic, 2 drachms., copper nitrate 20 grains, acetone 2 fl. oz., methylated spirit to 8 fl. oz. Nine weeks later the patient's rash had cleared except for an interdigital fissure and a localized area of superficial scaling from which *T. concentricum* was isolated. *H. T. H. Wilson*

Bogliolo, L. & Neves, J. A. **Researches on the Etiological Agents of the American Blastomycosis. II. Morphology and Systematic of the Agent of Posadas-Wernicke's Disease (so called Coccidioidomycosis).** *Mycopathologia.* The Hague. 1952, June 30, v. 6, No. 3, 137–60, 7 pls. & 19 figs. [19 refs.]

Coccidioides immitis, like some other fungi which cause specific systemic mycoses, was believed to belong to the protozoa, before it was known in saprophytic culture, and the generic name *Coccidioides* was based on the resemblance of the parasitic sporangium of the fungus to the protozoon

Coccidium. Its systematic position is uncertain but it has generally been assigned to the class of *Phycomycetes*.

The present authors consider that the fungus should be studied anew in saprophytic culture and its proper generic characters determined. In pursuance of this object, a study was made of the morphological characters of 11 strains of *C. immitis* in culture on Emmons's corn-meal agar, " Sabouraud with glucose or dextrose ", and potato-dextrose agar (Bacto). Hanging-drop micro-cultures were not used as they were considered to " constrain " the fungus.

The description of the macroscopic appearance of the cultures presents nothing new. Microscopically, " the characteristic and indeed the predominant fructification is represented by aleurias or aleurospores which are usually central . . . ". This implies that the authors interpret the catenulate spores, commonly called chlamydospores, as aleuriospores. In addition to the central " aleurias ", there are lateral forms which may be borne singly on the side of an exhausted segment of the parent hypha, or from a central aleuria or a fertile hyphal segment. They are rarely pediculate and they are sometimes arranged in the form of " thyrses " as in the ringworm fungi, but they are larger than the conidia (aleuriospores) of *Trichophyton* or *Microsporum*. A more complex sporiferous structure is formed by lateral branching from a hypha, with secondary branching almost at right angles, and such ramifications bear the aleuriophora, the organs of fructification. Other structures of the mycelium (not uncommon in many different fungi) observed were racquet hyphae, chlamydospores, terminal dilatations, spiral hyphae, pectinate bodies and structures recalling the favic chandeliers. [See also Negroni, this *Bulletin*, 1949, v. 46, 1174.]

On the basis of these observations the authors consider that *C. immitis* is closely related to the dermatophytes, and they assign it, together with *Paracoccidioides brasiliensis* and *Blastomyces dermatitidis*, to the genus *Aleurisma* Link, 1809, as *Aleurisma immitis*. The Latin diagnosis is appended.

The authors, apparently, have not taken into consideration the sporangial form in culture described by Baker and Mrak (*Amer. J. Trop. Med.*, 1941, v. 21, 589) and others. *J. T. Duncan*

Tarbet, J. E. & Breslau, A. M. **Histochemical Investigation of the Spherule of *Coccidioides immitis* in relation to Host Reaction.** *J. Infect. Dis.* 1953, Mar.-Apr., v. 92, No. 2, 183–90, 7 figs. [24 refs.]

In an earlier report, Tarbet *et al.* [this *Bulletin*, 1953, v. 50, 244] presented experimental evidence of the different cytological reactions of the animal host to infection by *Coccidioides immitis*, confirming the original observation of Ophuls (1905) that the infecting spores of the fungus and the recently liberated parasitic endospores provoke an invasion of polymorphonuclear cells, and the developing stages of the parasitic spherule, a reticulo-endothelial cell or monocyte reaction.

The object of the present study was to ascertain if these two different cytological responses could be ascribed to determinable chemical differences in the stages of the parasite which provoked them. For this purpose, the various developmental stages of the parasite, in sections of infected mouse tissue, were studied after staining with Korson's differential trichrome technique for nucleic acids, by Baker's acid hematin technique for phospholipid, and by Lison's *alpha*-toluidin blue reaction for mucopolysaccharide. The safranin-fast-green technique was also used in conjunction

with digestive procedures in the study of the cell wall of the parasite, especially in relation to the presence of chitin and cellulose.

Korson's staining method showed that ribonucleic acids were present in large amount throughout the entire developmental cycle of the parasite, which indicated continuous metabolic activity and no dormant stage. From this it can be concluded that the monocyte type of response was not related to a dormant phase of the parasite acting as an inert foreign body.

Baker's method showed that the thick walls of the large spherule forms were strongly positive for phospholipid while the covering of the sporangiospores was entirely lacking in this material. The thickness of the phospholipid layer was proportional to the size of the cell. From this observation it is concluded that the chemical interchange between the parasite and the host's tissues will be different in the case of the sporangiospores because of the absence of an intervening phospholipid layer, and this may explain the polymorphonuclear cell reaction to the sporangiospores. Alternatively, the phospholipid in the wall of the spherule may possess distinctive chemotactic properties for the monocyte elements of inflammation.

The results from Lison's technique indicated that the covering of the sporangiospores and the matrix material in which these lie in the sporangium contain a considerable proportion of mucopolysaccharide. The vacuoles of the larger spherules also contain this antigenic material, but in them it is separated by the cytoplasm and the spherule wall from contact with the host's tissues. The rapid influx of polymorphonuclear cells when sporangiospores are released and the invasion of the empty sporangial capsule may be accounted for if the material referred to contains a catalyst such as hyaluronidase or leucotaxine.

Tests of the spherular cell wall by the safranin-fast-green technique and digestive procedures showed, by comparison with eggs of *Ascaris* and with privet leaves, that chitin is probably present but not cellulose.

J. T. Duncan

KARRER, H. E. **Virulence of *Coccidioides immitis* determined by Intracerebral Inoculation in Mice.** *Proc. Soc. Exper. Biol. & Med.* 1953, Apr., v. 82, No. 4, 766–8. [12 refs.]

In previous studies on the infectivity of fungi for animals by experimental inoculation, various means have been employed to increase the probability of a lethal infection; as by lowering the resistance of the animal through exposure to X-rays [BRANDT, *Bull. Hyg.*, 1951, v. 26, 47], by adding gastric mucin to the inoculum [CAMPBELL and SASLAW, *ibid.*, 1950, v. 25, 924], by using the intracerebral route for inoculation [HOWELL and KIPKIE, *ibid.*, 1951, v. 26, 643, 775, 776], or by selecting particularly susceptible strains of the animal species [Howell and Kipkie, *ibid.*, 643, 775].

The present study was devised to find a method of measuring and comparing the virulence of strains of *Coccidioides immitis*; for this purpose, the death rate after intracerebral inoculation, computed as LD50 was accepted as a convenient measure of virulence. The cerebral route of inoculation was adopted and, for reasons of economy, albino mice were used although they are rather less susceptible to fungus infections than the coloured varieties.

Two strains of *C. immitis* were compared, and freely sporing cultures were used for the inoculations. It had previously been shown that the chlamydospore of the fungus is the infective element and not the dissociated, although viable, mycelial fragments, and when the proportion of spores in the fungal suspension is high, very small inocula are sufficient.

The survival time of the inoculated mice varied inversely with the magnitude of the inoculum, but death, in all fatal cases, occurred within the defined time of 30 days.

The 2 strains of *C. immitis* had a high degree of virulence for mice by intracerebral inoculation, and a statistical analysis of the data collected from the experiments showed the LD50 for the 2 strains to correspond to 1 to 6 and 1 to 9 fungal particles (spores and mycelial fragments) respectively. This may not indicate a significant difference of virulence, but if the range of dilutions of the inoculum and the numbers of mice used were sufficiently increased, the statistical analysis should give narrower limits for the LD50, by which small differences in virulence would be revealed. *J. T. Duncan*

Jervis, O. Blastomicosis Sudamericana observado en Guayaquil. II. Aspecto clínico. [**South American Blastomycosis in Guayaquil**] *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1953, Apr., v. 1, No. 2, 44–53, 3 figs.

Rodríguez M., J. D. A propósito de un caso de Blastomicosis Sudamericana observado en Guayaquil. I. Aspecto micológico. [**A Case of South American Blastomycosis in Guayaquil. I. Mycological Aspects**] *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1953, Apr., v. 1, No. 2, 39–43.

Machado Filho, J. & de Carvalho, Maria da C. M. Considerações em tôrno das localizações pulmonares da paracoccidioidose brasileira. [**Observations on the Development of the Pulmonary Localizations of Paracoccidioidomycosis in Brazil**] *Rev. Brasileira Tuberculose.* Rio de Janeiro. 1952, Sept.–Oct., v. 20, No. 143, 503–36, 14 figs. [58 refs.]

Recent reports have indicated the extent of endemic paracoccidioidomycosis in Brazil and the need for effective prophylactic measures which, in turn, depend upon the very early diagnosis of the infection. This is facilitated by the presence of characteristic skin and mucosal lesions, but, when these are absent, the disease involving the deeper organs is more difficult to detect, especially when asymptomatic.

The object of the present study was to clear up certain ambiguities in relation to the involvement of the lungs in Lutz's disease (paracoccidioidomycosis). The investigation was directed to (a) a tentative systematization of the radiological aspects of the lesions, with observation of their evolution; (b) a study of the literature bearing on the radiographic-anatomy and the structure of the lesions; (c) an estimation of the respiratory capacity; and (d) a therapeutic trial of cortisone.

The disease affects chiefly agricultural labourers and in the series of 10 cases studied in the present investigation, all of whom suffered from the pulmonary or tegmento-pulmonary forms of the disease, 8 were agricultural workers chiefly from rural areas, 1 a mechanic from the sub-rural zone and 1 a radio technician from the urban zone of Rio de Janeiro; all were of the White race. The predominant type of pulmonary lesion shown in 5 of the cases was nodular, in 3 fibrotic and in 2 infiltrative. The lesions were usually bilateral and symmetrical, distributed chiefly in the middle and lower lung fields, and linear shadows radiating from the lung root to the periphery were characteristic. The apices of the lungs were not involved and there was no indication of hilar lymphadenopathy or of large lung cavity.

Tentative treatment with cortisone was given by mouth, commencing with 300 mgm. on the first day, given in 4 doses of 75 mgm. every 6 hours;

thereafter, for 14 days, 100 mgm. were given daily in 4 doses of 25 mgm. In one case generalized oedema developed after 5 days of treatment, but this complication responded well to exclusion of salt from the diet and the administration of a mercurial diuretic. No other patient reported any untoward symptom and all experienced a marked feeling of well-being. The treatment did not provoke reactivation of quiescent lesions nor the development of new lesions. Its effect was to cause disappearance of the granulomata, and promote proliferation of the collagenous tissue and the growth of epithelial cells. The evidence of healing by fibrosis, although encouraging, was nevertheless rendered inconclusive owing to the variable conditions of the experiment, and further therapeutic tests on these lines are necessary.

The report is supplemented by brief clinical and radiological histories of the 10 cases, and the X-ray photographs illustrating them are of remarkable clarity.

An earlier report on the pulmonary lesions of paracoccidioidomycosis was made by Lacaz [this *Bulletin*, 1951, v. 48, 1144]. *J. T. Duncan*

Barros Saint-Pasteur, J. Estudio general de la Paracoccidioidosis brasiliensis. Su importancia en Odontología. (Acerca de una primera comunicación sobre Paradentosis Paracoccidioidica.) [**General Study of the Paracoccidioidomycosis of Brazil. Its Importance in Odontology. (Concerning a Primary Report on Paracoccidioidal Paradentosis)**] *Bol. Laboratorio Clinica "Luis Razetti"*. Caracas. 1952, July, v. 16, Nos. 37/38, 493–525, 2 figs.

Aleixo and Furtado [this *Bulletin*, 1949, v. 46, 283] described 5 cases in which infection by *Paracoccidioides brasiliensis* (Lutz's disease) appeared to have originated in unhealthy dental sockets, and they referred to an earlier report by Bogliolo on the development of paracoccidioidal granuloma in tooth sockets.

The present paper, a thesis submitted for the doctorate, deals with Lutz's disease in general and its importance to odontologists. Much of the text is devoted to an account of the history and literature of Lutz's disease, with particular reference to its occurrence in Venezuela, where it was reported for the first time by O'Daly in 1937. The greater part of the paper is occupied by a description of the dental diseases which predispose to the fungus infection.

Paradental disease may be divided into 3 types: gingivitis, which may be localized to a small dental area or involve the entire gum arch; paradentitis, a relatively benign process which affects the gum margin, the epithelial insertion, the periodontal membrane and the alveolar crest; and paradentosis, a more grave process which compromises the life of the tooth. The stages of paradentosis, taken in order, are diminished resistance of the gums, gingival infection, penetration and extension of the infection by the dental and periodontal lymphatics, injury to the highly vascular periodontal membrane, destruction of the cortical fibres remaining inserted in the cement with consequent destruction of the cementoblasts and death of the cement substance which becomes bathed in pus, disappearance of the cortical fibres attached to the bony alveolus, and local destruction of the osseous tissue of the alveolus.

Six cases of paradentosis associated with infection by *P. brasiliensis* are discussed and the dental lesions are illustrated by X-ray photographs which show the apical area to be the principal site of the paracoccidioidal infection.

Treatment with the sulphonamides, which has proved successful in the systemic disease, may not be effective in the paradentosal lesions because of the barrier to the penetration of the drug, imposed by a granulomatous tissue rich in collagen fibres. The prophylactic importance of constant attention to the hygiene of the mouth is stressed. *J. T. Duncan*

TROPICAL OPHTHALMOLOGY

i. Gaud, J. & Decour, H. Traitement de masse des conjonctivites saisonnières en milieu marocain (expériences de 1951). Introduction. [**Mass Treatment of Epidemic Seasonal Conjunctivitis in Morocco**] *Bull. Inst. Hyg. Maroc.* 1951, v. 11, Nos. 3/4, 233–6, 1 map.

ii. Bidart, J. & Racoillet, R. I.—Activité comparée de l'auréomycine et de la solufontamide associés ou non aux sulfamides. [**Comparative Action of Aureomycin and Solufontamide with or without Sulphonamides**] *Ibid.*, 237–46, 1 map & 2 figs.

iii. Ferrand, G. & Soyer, R. II.—Résultats comparés du collyre à la streptomycine et de la pommade à l'auréomycine. [**Comparative Results Obtained with Streptomycin Instillations and Aureomycin Ointment**] *Ibid.*, 247–62, 2 figs.

iv. Bardon, H. III.—Action comparée des instillations de streptomycine et de chloramine [**Comparative Action of Streptomycin and Chloramine Instillations**] *Ibid.*, 263–9, 1 fig.

i. Epidemic acute mucopurulent conjunctivitis due to infection by the Koch-Weeks bacillus is extremely common in Morocco. In the mass treatment of this conjunctivitis the authors have found that instillations of aureomycin are the most efficacious. Streptomycin is also efficacious but inferior to aureomycin, and other drugs are useful, but to a less extent, in the following order, chloramine, " Solufontamide " and 1 per cent. zinc sulphate. They also found that sulphonamides by mouth reinforce the action of aureomycin and solufontamide. Details of dosage are not given.

ii. The authors carried out an investigation on the treatment of epidemic acute conjunctivitis on the Moroccan population of Fédala. In their experience the following 2 lines of therapy were worthy of retention:

(1) aureomycin with or without the combination of thiazimide [sulphathiazole] brought about almost total cure and was the best method of treatment. Aureomycin was used in the form of an ointment 1 per cent. strength and applied twice a day for 5 days;

(2) Solufontamide in combination with thiazimide proved effective for the first course, but the second course of treatment was less efficacious. Solufontamide was used in the form of drops 33 per cent. in strength and instilled twice a day for 5 days. Thiazimide was also given for 5 days, 2 to 6 tablets a day, depending upon the age of the patient.

iii. In 1951 during the epidemic months September to November the authors carried out a survey on the treatment of epidemic conjunctivitis in the southern part of Morocco with 1 per cent. streptomycin drops and 1 per cent. aureomycin ointment. The drugs were used twice a day for 5 days and a second course of treatment was carried out with about one month's interval. The drugs were used both for prophylaxis as well as for treatment.

The authors found that aureomycin was the more efficacious drug although the results with streptomycin were also striking. The effects of aureomycin were of much longer duration although the cost of treatment was considerably greater than that of streptomycin.

iv. A comparison of the treatment of acute conjunctivitis with a 1/125 solution of streptomycin and 1/1,000 chloramine was carried out by the author in Morocco. Instillations were given twice a day for 5 days with a second course of treatment within a maximum of one month's interval.

The action of streptomycin was found to be remarkable and was superior to that of chloramine, which however is a drug not to be disregarded. The author found that 2 days' treatment with streptomycin equalled 4 days' treatment with chloramine and that its prophylactic value was of equal importance with its therapeutic effect. *E. W. O'G. Kirwan*

NATAF, R. **Le trachome. Historique—clinique—recherches expérimentales et étiologie—thérapeutique—prophylaxie.**

This book was reviewed on p. 590.

MITSUI, Y. **Use of the New Antibiotics in the Treatment of Trachoma.** *Kumamoto Med. J.* 1952, Mar. 30, v. 4, Nos. 3/4, 105–11, 3 figs.

In the author's experience, proper treatment of acute trachoma with terramycin or aureomycin " brings about a radical cure without exception ". An 0·1 per cent. ointment applied 4 times daily seems to be the minimum dosage. There seems to be no limit with regard to the maximum dosage. In the acute stage a clinical cure results in the course of 2–3 weeks and a further " after cure treatment " for about 2 weeks results in a radical cure. Combination with a small dosage of sulphonamide and also with hyaluronidase may be beneficial.

Most trachoma in schoolchildren is at an early stage and the following line of treatment is recommended for them: an ointment of 0·5 or 1·0 per cent. terramycin or aureomycin thrice daily for 4 weeks as a first course of treatment. Examination is made after 3 months. A repetition of the same course is recommended in cases which have not been cured. In cases which have been little improved, sulphonamides in combination with the antibiotics and surgery are recommended. In chronic trachoma an essential cure is brought about in most cases after topical treatment with 0·5 per cent. terramycin or aureomycin applied thrice daily for a month or so. In some cases treatment for a few days only is sufficient to effect a cure; in others, treatment for 2 months or more is necessary. Surgical treatment assists in the elimination of secondary stages. In corneal complications, acute pannus and ulceration of the cornea can be cured in a short time with antibiotics, but prolonged treatment is required to obtain a radical cure of the disease. *E. W. O'G. Kirwan*

BADIR, G. & KAMEL, S. **Aureomycin in the Treatment of Trachoma and certain other Conjunctival Infections in Egypt. A Preliminary Report.** *Bull. Ophthalm. Soc. Egypt.* 1950, v. 43, Session 47, 22–34.

In the authors' first series of experiments, the effect of aureomycin was tried on 7 patients, and also on 2 baboons, suffering from trachoma which was free from infection with pathogenic organisms. In the second series

the effect of aureomycin on the conjunctival flora and the effects of elimination of the bacterial infections of the conjunctiva on the residual signs of trachoma were tried on 14 selected patients.

The outcome of these experiments showed no immediate effect on the clinical signs of trachoma, yet aureomycin seemed to promote early cicatrization in the majority of cases not complicated by secondary infection and caused a diminution in the number of inclusion bodies. In the secondary infections it did not seem superior to the sulphonamides, penicillin, zinc sulphate or diamidines. The effect of aureomycin has yet to be tried on cases of acute conjunctivitis during the seasonal epidemics and a large number of cases must be treated with this antibiotic before a definite conclusion can be reached. The results obtained on the few cases of trachoma gave the impression that the use of aureomycin was a good step forward in the treatment of this endemic disease, and that it might well prove to be the ideal drug. Detailed results are shown in 4 tables.

E. W. O'G. Kirwan

Nguyen-Dinh-Cat. Essai de traitement du trachome par la terramycine. [**Trials of Terramycin in the Treatment of Trachoma**] *Extrême-Orient Méd.* Hanoi. 1952, Jan.–May, v. 5, No. 1, 185–93.

Fourteen patients suffering from severe forms of trachoma were treated by the author with topical terramycin after previous curetting of the granulations. Very encouraging results were found, comparable with those obtained with aureomycin. In early trachoma, terramycin produced improvement in 3–5 days. In the florid forms it brought about cure by cicatrization in 6 weeks to 2 months. In the minor complications of blepharitis and pannus tenuis it has proved valuable. As a local application it was well tolerated and in spite of prolonged treatment did not produce irritation of the bulbar conjunctiva or corneal epithelium and allergic reactions were not observed.

Although it cannot be considered a specific in the cure of trachoma, terramycin is without doubt a very valuable remedy in the campaign against trachoma.

E. W. O'G. Kirwan

Remy, F. Evolution du trachome sous l'influence de médications trophiques, [**Effect of "Trophic Substances" on Trachoma**] *Bull. Inst. Hyg. Maroc.* 1951, v. 11, Nos. 3/4, 271–9.

In 1950 an investigation was carried out by the author in Morocco on trachomatous patients resistant to the ordinary therapeutic drugs, which did not include aureomycin or terramycin. He used various substances in the form of instillations which he classified under the name of "trophic solutions". These included liver extract, placental extract, cod liver oil and preparations containing vitamins B and C. The experiments were carried out on 700 schoolchildren attending 3 schools in the region of Fez. He formed the following conclusions: the results were always satisfactory but the best results were obtained with liver extract and cod liver oil. The advantages of the treatment were its simplicity, the low cost, and the treatment could be carried out by the teachers in the schools.

E. W. O'G. Kirwan

MISCELLANEOUS DISEASES

WOLTER, A. Enfermedades exóticas y sus relaciones con la estomatología. A base de algunos cuadros elegidos de enfermedades exóticas. [**Stomatology and Exotic Diseases**] *Med. Colonial.* Madrid. 1953, June 1, v. 21, No. 6, 606–20, 13 figs.

The author, who writes from Berlin, describes some of the tropical diseases in which lesions of the mouth and nasopharynx occur, such as gingivitis, pyorrhoea, nodules and ulcers of leprosy, the milia and nodules of verruga peruana, the ulceration and necrosis of espundia, blastomycotic disease of the lips, the secondary generalization of yaws and the sequela of gangosa, the glossitis, stomatitis, aphthae and ulcers of sprue and the lesions of rhinoscleroma and rhinopharyngitis. Photographs illustrating some of these lesions are reproduced, but the article does not contain anything not already familiar to readers of this *Bulletin*.

H. Harold Scott

CHAMBERS, H. D. **The Syndrome called 'Vomiting Sickness'.** *West Indian Med. J.* 1953, Mar., v. 2, No. 1, 37–42.

From a clinical analysis of 60 patients sent to the Kingston Public Hospital, Jamaica, with a provisional diagnosis of vomiting sickness, the author shows that the term covers a number of diseases which should be specifically named and not relegated to a ragbag labelled with the name of a single symptom, which may not even itself be prominent. Hence, his 60 cases include those found suffering from pyelitis, gastritis and gastro-enteritis, poisoning by ackee, antimony, mercury and phosphorus, fish-poisoning and subtertian malaria. He suggests "acute nutritional (parenchymal) hepatitis" for some of these. [Professor K. R. HILL has described a serous hepatitis in Jamaican children (see this *Bulletin*, 1952, v. 49, 437; 1953, v. 50, 329) which may be allied to, perhaps identical with, the author's nutritional hepatitis.] *H. Harold Scott*

WILKINSON, J. **The Pathology and Etiology of Onyalai.** *East African Med. J.* 1953, May, v. 30, No. 5, 193–209, 1 fig. [41 refs.]

This paper deals with the pathology and aetiology of onyalai, of which little is known. It is essentially a bleeding disease characterized by a severe drop in the platelet count, and the principal changes are the presence of haemorrhages or purpuric spots in the skin, mucous membranes and viscera. Because it is a thrombocytopenia, the bleeding time is prolonged, but not the clotting time. An anaemia is to be expected, its severity depending on the amount of blood lost. Although the circulating blood platelets are reduced, usually below 50,000 per cmm., megakaryocytes are present in normal numbers in the bone-marrow in most of the cases so far recorded. The prothrombin time is normal and other blood investigations usually reveal nothing of note. Perhaps one of the most interesting features of this disease is the blood-filled bullae more commonly seen in the mouth and on the tongue than on the skin. They form rapidly and disappear almost as quickly. Their numbers and size vary, and cases are occasionally found in which no bullae can be demonstrated in the mouth or nose.

The author discusses at some length the theories of normal haemostasis and of the pathogenesis of onyalai. The theory regarded as being the most acceptable in the case of the disease is that postulating the production of a toxic substance by the spleen: it is suggested that this substance

(a) depresses platelet formation in the bone-marrow and (b) inhibits normal capillary vaso-construction. The hypothetical stages in this process are set out in a figure.

Regarding the aetiology of the disease, there is less to mention. Efforts to find a causative organism have been fruitless; certainly malaria and the spirochaete of syphilis do not appear to be related to the condition. Although the disease often occurs in apparently well-nourished persons, a few workers have regarded it as being due to a deficiency in one or other vitamin, especially in C or K. Similarly it is doubtful whether there is sufficient evidence to support the view that a poisonous or toxic factor is present as a result of medicine supplied by the African witch doctor, since one sees many cases in which there does not appear to be any evidence of this. There is perhaps more support for the theory that onyalai is an allergic state, and recently claims of success with antihistamines have been made. The bullae and even the purpura are perhaps suggestive of an allergic phenomenon. Many cases of onyalai seem to follow the administration of certain European drugs, especially organic arsenicals. Several cases have now been recorded in which the patient has succumbed to a condition indistinguishable from onyalai when given neoarsphenamine treatment.

Nevertheless, the true nature of onyalai still eludes us. [For previous work on onyalai by the same author, see this *Bulletin*, 1953, v. 50, 759, 854.]

Michael Gelfand

Sakihara, H. **A Case of Melioidosis in a Japanese Soldier in Malaya.** *Japanese J. Med. Sci. & Biol.* 1952, Dec., v. 5, No. 6, 425–32. [14 refs.]

Deschiens, R., Lamy, L. & Estival, J. Action de la cortisone dans l'éosinophilie parasitaire. [**Action of Cortisone in Eosinophilia of Parasitic Origin**] *Bull. Acad. Nat. Méd.* 1953, v. 137, Nos. 19/20, 306–8.

From the inmates of the Brazzaville gaol were selected 11 subjects with gross parasitic infestation and an eosinophilia of 23–61 per cent. representing 1,426–7,198 eosinophiles per cmm. All received 100 mgm. of cortisone at 48-hour intervals, a total of 700 mgm. in a fortnight. There was no significant change in the eosinophile counts as a result.

This finding might be of value in the differential diagnosis from tropical eosinophilia where the eosinophile count was found to be significantly depressed after injections of cortisone [this *Bulletin*, 1953, v. 50, 760].

It is possible that the eosinophilia following parasitic infestation might be reduced by higher doses of cortisone than were used in the present experiment; but this increased dosage might not be without risk in man, and such studies should be confined to laboratory animals.

H. T. H. Wilson

PROTOZOOLOGY: GENERAL

Sterger, S., Kocijančič, K. & Šilc, M. Primer toksoplazmoze pri nas. [**First Confirmed Case of Toxoplasmosis in Yugoslavia**] *Zdravstveni Vestnik.* Ljubljana. 1953, v. 22, No. 5, 139–43, 4 figs. [14 refs.] English summary.

Tilden, I. L. **Congenital Toxoplasmosis. Report of a Fatal Case in Hawaii.** *Hawaii Med. J.* 1953, May–June, v. 12, No. 5, 355–8, 3 figs.

Miller, Louise T. & Feldman, H. A. **Incidence of Antibodies for Toxoplasma among Various Animal Species.** *J. Infect. Dis.* 1953, Mar.–Apr., v. 92, No. 2, 118–20.

The authors used the dye test of Sabin and Feldman to look for *Toxoplasma* antibodies as serological evidence of infection in 298 animals of 6 species: these included stray dogs and cats, 2 herds of cattle and laboratory-bred albino rats, guineapigs and rabbits.

The results are shown in a table, which indicates that, with titres of 1/16 or higher as evidence of infection, all of 54 rats and of 10 cattle from one herd were negative. There was only 1 positive in 22 rabbits (4·5 per cent.), but 14 in 51 guineapigs (28 per cent.), 15 of 44 cats (34 per cent.), 30 of 51 dogs [shown in the text as 20] (59 per cent.) were positive.

Low titres, up to 1/4, considered as negative, were found in the case of 29 cattle from the second herd of 66, in 9 cats, 4 dogs and 5 guineapigs. Thus all the cattle serum would be regarded as negative and it might be concluded that they are not often infected and—if this is correct—that cow's milk is not likely to be a significant hazard for human beings in this respect.

The discrepancy between the high percentage of findings in guineapigs and the low or negative findings in laboratory rats and rabbits is not explained, but the suggestion is made that since guineapigs are usually housed in much larger groups, animal-to-animal transmission is more likely to occur. The findings in rabbits agree with those of Sabin, but the authors refer to the percentage of 9·4 positive dye tests among wild hares in Denmark reported by Christiansen and Siim [this *Bulletin*, 1951, v. 48, 1150].

Toxoplasma had been demonstrated in dogs by Jacobs and Jones [*ibid.*, 1950, v. 47, 1229] and Grocott [*ibid.*, 1951, v. 48, 88]. The present authors point out that their own findings of a high percentage of infection in domestic dogs and also in cats suggests that they may be important reservoirs for human infection; but this frequency complicates the problem of incriminating a particular dog or cat in relation to human disease, and two cases are reported where this difficulty arose. [In the original paper, the reference to Jacobs and Jones is incorrectly quoted.]

H. J. O'D. Burke-Gaffney

Sexton, R. C., Jr., Eyles, D. E. & Dillman, R. E. **Adult Toxoplasmosis.** *Amer. J. Med.* 1953, Mar., v. 14, No. 3, 366–77, 2 figs. [25 refs.]

The authors review the literature on the discovery of infection by *Toxoplasma gondii*, and summarize reports of 5 cases in adults in which the parasites were found. They report a fatal case in an adult laboratory worker.

A white, female, aged 47 years, had worked for 2 years before her illness in a laboratory carrying out experimental infections of animals with *Toxoplasma gondii*. For about 4 months she had been tired and lethargic, and her illness began with malaise and chills, pains in the joints and lethargy. A doctor prescribed chloramphenicol but she became worse with fever and delirium and was admitted to hospital on 7th April, 1951, the fourth day of illness. In addition to fever and delirium there was a general maculo-papular rash which spared only the palms, soles and the scalp. There were some larger, raised, red, haemorrhagic lesions on the abdominal wall. The pulse rate was increased, and the blood pressure was rather low but fluctuated much during the illness. Later, râles were heard at the right lung base, and protein appeared in the urine. There was a leucopenia at

first, with proportional increase in neutrophiles, and a reduced erythrocyte count. The cerebrospinal fluid showed a slight increase in protein but no increase in cell content. In the later stages of the illness there was continued high fever, some convulsions with developing coma, persisting râles in the chest, a fading of the rash, some bleeding from the large bowel, and depression of the levels of plasma Na, K and Cl.

Treatments were attempted with aureomycin, dihydrostreptomycin, penicillin, with sulphonamide, and with cortisone and electrolyte replacement, but there was no response, and the patient died on 13th April.

A full post-mortem examination could not be made but the main findings were that the heart muscle was soft, and on section showed focal myocarditis with mononuclear infiltrations, and in these areas some of the muscle fibres contained cyst-like areas packed with small spherical organisms. The lungs showed no parasites in the cells of the alveoli, but there was interstitial infiltration with fibroblasts and mononuclears. The liver showed fatty change. There was blood in the lumen of the descending colon.

Serological studies were of great interest in this case since 3 specimens of serum before illness could be tested by the dye test of Sabin and Feldman. They were negative. A specimen on the 4th day of illness showed a titre of 1/16, and this had increased by the 8th day to 1/256.

Though the authors found animal inoculation too slow in giving assistance in diagnosis during life they obtained positive results in mice by intraperitoneal or intracerebral inoculation of blood, cerebrospinal fluid, and emulsified brain, liver and spleen tissue from the patient.

Clinical diagnosis is difficult in a disease with such protean manifestations. The authors say that toxoplasmosis should be considered in a patient with fever, maculo-papular rash, signs of pneumonia, and evidences of central nervous system involvement. The presence of polymorphonuclear leucocytosis with negative bacteriological findings strengthens the possibility. Absence of splenomegaly, and sparing of the palms, soles and scalp by the rash may help in reaching a diagnosis. Confirmation may be obtained by finding the organisms in a skin or muscle biopsy, or by sputum examinations. Animal inoculation of sputum may prove positive. A rising titre in the dye test, or in the complement-fixation test, would be confirmatory.

The authors consider that there is experimental evidence of some therapeutic effect from sulphonamides, aureomycin, and the sulphone drugs. They point out that various routes of infection have been suggested including by the agency of arthropods, by droplet infection, or from the bowel to the mesenteric glands. The hazard to laboratory workers is demonstrated.

S. Bell

Eyles, D. E. & Coleman, Nell. **Synergistic Effect of Sulfadiazine and Daraprim against Experimental Toxoplasmosis in the Mouse.** *Antibiotics & Chemotherapy.* New York. 1953, May, v. 3, No. 5, 483–90, 3 figs.

The authors have previously reported that daraprim was active against toxoplasmosis in the mouse, prolonging life or effecting cure in some cases [this *Bulletin*, 1953, v. 50, 158]. They concluded, as a result of other tests [*ibid.*, 568], that sulphadiazine was the most effective sulphonamide in the treatment of this infection. A pyrimidine structurally related to daraprim was found by Greenberg and Richeson [this *Bulletin*, 1950, v. 47, 1186] to potentiate the action of sulphadiazine against *P. gallinaceum* and this observation has been exploited in the present experiment.

Toxoplasma gondii obtained from a wild rat was used in dosage of 20,000 organisms to inoculate young mice so that death of control mice took place in 7 days. The drugs were administered in the diet, starting immediately after inoculation, for a period of 14 days. Observation of treated animals was continued for 42 or 84 days, after which the animals were killed and suspensions of brain were inoculated to clean mice, and survivors of 2 further passages were observed for 28 days. Viscera were also examined when the mice were killed, to establish whether cure had been effected. Some mice which had survived 42 days after the original inoculum were challenged with the same amount of infective material to determine if immunity had been developed. The size of the inoculum influenced greatly the number of mice which were cured. The time at which therapy was begun was also found to affect the results which were most favourable when treatment was started early after infection.

The authors concluded from the data obtained that there was a definite synergic action between daraprim and sulphadiazine, and express the hope that the combination will prove of value in treatment of the human disease, but further data on the toxic levels of daraprim are required. The drugs produced cure in approximately 53 per cent. of about 300 mice when diets containing 1·12 mgm. per cent. or more of daraprim along with 5 mgm. per cent. or more of sulphadiazine were given. Indications were obtained that diasone and daraprim acted in synergic fashion, and paludrine [proguanil] which alone was inactive, also potentiated sulphadiazine to a slight extent.

J. D. Fulton

Garin, J. P. Toxoplasmose expérimentale aiguë de la souris. Échec du traitement par l'histoplasmine. [**Failure of Histoplasmin Treatment of Experimental Acute Toxoplasmosis in Mice**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 323–4, 1 fig.

The following is a translation of the author's summary:

A solution of a culture of *Histoplasma capsulatum* on Long's medium, injected into mice inoculated with *Toxoplasma gondii* neither cured nor protected them against this fatal infection. This same solution (histoplasmin) did not prove toxic to control animals, even at a daily subcutaneous dose of 1 ml.

H. J. O'D. Burke-Gaffney

Garin, J. P. Toxoplasmose expérimentale aiguë de la souris. Échec du traitement par la terramycine. [**Failure of Terramycin Treatment of Experimental Acute Toxoplasmosis in Mice**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 325–7, 1 fig.

The following is a translation of the author's summary:

Terramycin used in a fresh buffered solution subcutaneously at a dose of 100 to 200 mgm./kgm. daily failed to protect or to cure a batch of 24 mice inoculated with a dose of ascitic fluid infected with a strain of *Toxoplasma* which was fatal to control mice in 5 days. It was able only to prolong survival of 7 animals for 2 to 16 days. This agrees with the conclusions of Puech [this *Bulletin*, 1952, v. 49, 1000] and of Grassi and Kass, whose papers were not available until after our experiments were completed.

[See also Eyles and Coleman, this *Bulletin*, 1953, v. 50, 569.]

H. J. O'D. Burke-Gaffney

Dvořák, J. Essai de diagnostic et de traitement de la pneumonie atypique parasitaire causée par le *Pneumocystis carinii* chez les nourrissons. Communication préliminaire. [**Study of Diagnosis and Treatment of Atypical Pneumonia in Infants Caused by** *Pneumocystis carinii*] *Schweiz. med. Woch.* 1953, Apr. 11, v. 83, No. 15, 354–6. [13 refs.]

In 1942 van der Meer and Brug described the clinical features of infection with *Pneumocystis carinii* in children [this *Bulletin*, 1944, v. 41, 152] and in 1951 Vanek studied the post-mortem changes in children who had died from the disease [*ibid.*, 1952, v. 49, 194]. Very few other reports appear to have been made, however, and in this paper 5 more cases in infants are described. The outstanding clinical features in these were cyanosis, an increased respiratory rate (90–125 per minute), a moderate degree of pyrexia, radiological changes suggesting an interstitial bronchopneumonia, and failure to respond to treatment with penicillin, streptomycin or aureomycin. At post-mortem examination alveoli were found to be filled with masses of mucus in which there were dividing forms of the parasite. The alveolar septa were infiltrated by lymphocytes and plasma cells. No other organisms known to cause pneumonia could be isolated. In two cases in which the diagnosis was reached on clinical grounds only, recovery followed treatment with 5 mgm. mepacrine daily for 6 days, followed by 5 mgm. plasmoquine daily for a similar period. [The daily doses of mepacrine (*atébrine*) and plasmoquine are shown respectively as "2 × 0·0025" and "5 × 0·001": if these are, as they seem to be, fractions of a gramme, the dose of mepacrine seems to be extremely small. See also this *Bulletin*, 1952, v. 49, 908; 1953, v. 50, 250.]

A. W. Woodruff

Jírovec, O., Soyka, O., Zázvorka, Z. & Voldřich, L. Tři nálezy vzácného parasita rodu *Sergentella* u člověka. [**Three Observations of Rare Parasites of the** *Sergentella* **Genus in Man**] *Československ. Hyg., Epidemiol., Mikrobiol.* Prague. 1953. v. 2, No. 2, 111–14, 4 figs. on pl. German summary (5 lines).

See also this *Bulletin*, 1953, v. 50, 856.

ENTOMOLOGY AND INSECTICIDES: GENERAL

[Papers on the toxic effects of insecticides in man are abstracted in the *Bulletin of Hygiene* under the general heading of Occupational Hygiene and Toxicology.]

Vermeil, C. *Aedes vittatus* Bigot 1861, *Culicide* nouveau pour la Tunisie. [*Aëdes vittatus* **Recorded for the First Time in Tunisia**] *Bull. Soc. Path. Exot.* 1953, v. 46, No. 3, 338–9.

Leví-Castillo, R. Nota sobre cuatro especies del género *Haemagogus*, Williston 1896 que son propias de la América Central (Diptera-Culicidae). [**Notes on Four Central American Species of** *Haemagogus*] *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1953, Apr., v. 1, No. 2, 15–24, 4 figs.

The English summary appended to the paper is as follows:—

"Descriptions are effected of four species of Haemagogus mosquitoes of Central America: H. (H) iridicolor, Dyar 1921; H. (H) argyromeris, Dyar

& Ludlow 1921; H. (H) regalis Dyer & Knab 1906 and H. (H) mesodentatus Komp & Kumm 1938, species are described in a systematical study of the larvae, adults and male terminaliae, giving larval habitat and geographical distribution."

Kirk, R. & Lewis, D. J. **Taxonomy of the Ethiopian Sandflies** (*Phlebotomus*). **V.—On *Phlebotomus africanus* Newstead, 1912.** *Ann. Trop. Med. & Parasit.* 1953, June, v. 47, No. 2, 126–31, 2 figs.

Sabrosky, C. W. **The Scientific Name of the Screw-Worm, with a Note on *Paralucilia fulvicrura* (Diptera, Calliphoridae).** Reprinted from *Proc. Entom. Soc. of Washington.* 1953, Feb., v. 55, No. 1, 36–8.

For many years the majority of authors (not by any means all) failed to observe that there are two rather similar species of *Cochliomyia* (or *Callitroga*) in the warmer parts of the Americas. The larva of the screw-worm fly is always parasitic in large mammals, the other insect breeds only in carcasses, but for a number of years both were referred to as *C. macellaria*. The distinction of the 2 was finally brought out by Cushing and Patton [this *Bulletin*, 1934, v. 31, 359], who showed clear anatomical differences both in larvae and adults. They failed, however, to study the many specimens, preserved in museums in London and Paris, that had been named by earlier dipterists, and made the unfortunate decision that the parasitic form must be described as new and gave it the name *americana*. Aubertin and Buxton [*ibid.*, 1935, v. 32, 665] showed that the earliest specific name of the parasitic fly is *hominivorax* Coquerel, 1858: original material is in London (British Museum), bred from a living convict at Cayenne. American authorities, giving no reasons, announced that they would adopt *americana* as the name of the parasitic insect, it being generally accepted that the non-parasitic insect breeding in carcasses is *macellaria*.

In the present paper an American dipterist of established reputation, who has gone to the trouble of looking at the material in Paris, concludes that " the correct scientific name of the screw-worm of the New World, hitherto called *Cochliomyia americana* or more recently *Callitroga americana*, is *Callitroga hominivorax* (Coquerel) ". *P. A. Buxton*

Klock, J. W., Pimentel, D. & Stenburg, R. L. **A Mechanical Fly-Tagging Device.** *Science.* 1953, July 10, v. 118, 48–9, 1 fig.

Wharton, G. W. & Fuller, H. S. **A Manual of the Chiggers. The Biology, Classification, Distribution, and Importance to Man of the Larvae of the Family Trombiculidae (Acarina).** *Mem. Entom. Soc. Washington.* 1952, No. 4, pp. viii+185, 17 figs. [23 pp. refs.] [$6.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1953, Apr., v. 41, Pt. 4, 50.]

The information on which this monograph is based has largely been drawn from the literature, but the results of certain original investigations that supplement previously existing knowledge are included. Introductory sections on the relationship of Trombiculid larvae to tsutsugamushi disease and to dermatitis in man, domestic animals and poultry and on the control of these larvae, and somewhat fuller information on their anatomy and bionomics (with notes on those of the subsequent stages of the life-cycle) precede the main section of the book (pp. 40–105), which deals with classification. This comprises keys to sub-families, genera and subgenera,

definitions of them, and lists of the species; the full synonymy of each species is given with references to the literature on it (in which the types of information in the individual papers are indicated) and records of its distribution and hosts. There are also a faunal list showing the species known from various countries, a list of hosts showing the species found on each, and notes on collecting and culture methods and on seasonal, diurnal and ecological distribution.

Dorman, S. C. & Hall, W. E. **An Improved Spray Tunnel Method for Laboratory Tests.** *J. Econom. Entom.* 1953, Feb., v. 46, No. 1, 151–3, 6 figs.

Rogers, E. F., Brown, H. D., Rasmussen, I. M. & Heal, R. E. **The Structure and Toxicity of DDT Insecticides.** *J. Amer. Chem. Soc.* 1953, June 20, v. 75, No. 12, 2991–9, 1 fig. [Refs. in footnotes.]

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

Medical Research Council. **The Sterilization, Use and Care of Syringes by a Committee appointed by the Medical Research Council** [Wilson, G. S., Chairman]. *M.R.C. War Memorandum No. 15.* 23 pp., 8 figs. [47 refs.] 1945. (Reprinted March 1953 with Minor Amendments.) London: H.M. Stationery Office. [9d.] [Summary appears also in *Bulletin of Hygiene.*]

This memorandum was issued in 1945 and is now reprinted with minor amendments. There has been abundant evidence, since its first publication, that there is still much carelessness in the sterilization of syringes and needles, and that this continues to be a serious factor in the spread of hepatitis. Readers will wish to be reminded that the memorandum is again issued; it should be read by all persons who are responsible for sterilization technique. *Charles Wilcocks*

Gorgas Memorial Institute. **Annual Report of the Gorgas Memorial Laboratory, 1952** [Siler, J. F., President]. 23 pp. 1953. Washington: Govt. Printing Office.

This report, as is usual, contains much technical matter of general interest, genuinely enabling the reader to understand the scientific progress made. Work which has been done on the following subjects appears to have been published elsewhere: the changing reaction of *A. albimanus* to DDT; forest mosquito studies and the taxonomy of *Aëdes leucocelaenus*; the taxonomy of *Phlebotomus* species; notes on herpes simplex and on BCG vaccination. A detailed progress report is given on the Chagres River experimental malaria control project, the later happenings in which do not seem to have been published. The scheme was started in 1929, and now provides a contrast between the results of (a) prophylactic treatment with aralen [chloroquine] and DDT application; (b) aralen prophylaxis only, and (c) the voluntary unorganized use of aralen prophylaxis. The last two systems give results which at first sight compare favourably with the first, but the highest bi-monthly and cumulative parasite rates are seen in an area of the last regimen.

Other points of interest noted include the demonstration of yellow fever immune bodies in 5 of 85 squirrel marmosets, 6 of 45 spider monkeys, 1 of 35 night monkeys, and among non-primates in 1 pygmy anteater and 2 agoutis, though the significance of the last 2 species is uncertain. The organism of Rocky Mountain spotted fever, *Rickettsia rickettsi* was isolated, for the first time in Panama, from two patients with the disease and from 11 adult ticks of the species *Amblyomma cayennense*.

The Institute has a scientific staff of 7 working in a central laboratory and 2 field stations; the nature of the work is wide in scope and distinguished in its detail. The report is interesting and deserves reading for its own sake as well as for a record of the progress of a particular institution.

G. Macdonald

Poindexter, H. A. **Epidemiological Survey among the Gola Tribe in Liberia.** *Amer. J. Trop. Med. & Hyg.* 1953, Jan., v. 2, No. 1, 30–38.

The Gola Tribe is a very primitive group in the Western Province of Liberia. Some 3,000 members were examined by a clinician who had behind him the resources of a good laboratory, and whose object was to study the nosology of these isolated people having little contact with even the fringes of scientific medicine. The results of the survey are too full for complete abstraction, but its scope may be judged from the following notes on the subjects handled.

Malaria. The parasite rate among adults was 11 per cent., among girls 13 per cent. and among boys 25 per cent. *Plasmodium falciparum* was present in 97 per cent. of films examined, and *P. malariae* in 3 per cent. Neither *P. vivax* nor *P. ovale* was seen.

Treponematosis. 20 per cent. of 1,500 Kahn reactions were positive; clinical yaws was common.

Intestinal helminthiasis. Ascaris and hookworm eggs were very common; *Strongyloides stercoralis* larvae, *Trichuris trichiura* eggs and *Enterobius vermicularis* were also seen.

Dermatitis and dermatoses. 32 per cent. of the people showed one or more types of skin disease, the commonest forms being mycoses and tropical ulcer or pyoderma without scabies; scabies, yaws, leprotic ulcers and other conditions were encountered. The clinical diagnosis and causal fungus of 461 mycotic lesions are classified, as also the specific cause of 381 non-mycotic lesions and the clinical diagnosis of 131 others.

Non-syphilitic infection of the genito-urinary tract. The clinical condition in 65 female and 101 male patients is recorded.

Red cell fragility tests. No difference was found between malarial and non-malarial bloods.

Sicklaemia tests. Sickling trait was found in 19 per cent. of 100 children.

Tuberculin patch tests. 4 per cent. of 100 adolescents were positive.

Mean white cell count. Between 5,000 and 6,000 per cmm.

Mean red cell count. 3,850,000 per cmm.

Coagulation time and bleeding time. 4·6 minutes and 2 minutes as measured by a given technique.

Dental defects. Some defects present in 11 per cent.

It is stated [but without detailed supporting data] that " only 20 per cent. of the products of conception " reach 6 years of age, and also that the expectation of life is 39 years. [To make these statements compatible it must be assumed that the proportion of antenatal deaths is very high.] A condition called " Open mole " characterized by widened sagittal sutures,

pulsating anterior fontanelle, high blood pressure and sometimes increased intracranial pressure, is briefly referred to as being common and not conforming to any known syndrome. *G. Macdonald*

Brown, J. S. **Some Features of Ganda X-Ray Anatomy.** *East African Med. J.* 1953, Apr., v. 30, No. 4, 145–54, 15 figs.

Many Ganda subjects, not suffering from any detectable disease, show X-ray anatomical appearances outside the range of what would be considered normal in Europeans. In this paper, which will be of interest to radiologists and anatomists in other parts of Africa, common " normal variants " are described and illustrated by line tracings. It appears that, in this population, some structures, while developing to a normal size, tend to retain in adult life the proportions, shape and configuration characteristic of the infant. *Dean Smith*

Ketterer, W. A. **Village Polyclinics in Middle Java.** *Pub. Health Rep.* Wash. 1953, June, v. 68, No. 6, 558–62, 2 figs.

The author gives a picture of disease as seen in an 11-day visit to two mission dispensaries in rural Java. Diagnosis was generally clinical, but reinforced by some laboratory examinations, and was made difficult by a complicated language barrier and by the multiplicity of infections in single individuals. The complaints of 883 persons, and their diagnoses, are tabulated. The chief causes of sickness were yaws (23·2 per cent.), malaria (16·0 per cent.), and ulcers (14·7 per cent.). Other conditions of great social significance were tuberculosis, trachoma and frank avitaminosis, which caused 8·0, 4·2 and 7·6 per cent. of the patients to seek treatment. The author comments on the great importance of tuberculosis, pleading that it should have the emphasis now given to the less common leprosy, and for the management of which there is little provision.

The author is an officer of the U.S. Public Health Service working for the Mutual Security Agency, and concludes that preventive work most deserves support. Public education, staff training and campaigns against malaria, yaws and tuberculosis deserve first attention. *G. Macdonald*

Bulletin of the National Society of India for Malaria and Other Mosquito-Borne Diseases. (Delhi: 22 Alipore Road. Subscription rates, yearly Rs. 15; Single copy Rs. 3.)

This Society was formed recently to advance and integrate knowledge and investigation of these diseases. The President of the Society is Lt.-Col. Jaswant Singh, who is also Director of the Malaria Institute of India.

The first issue of the *Bulletin of the National Society of India for Malaria and other Mosquito-borne Diseases* was published in January, 1953, and contained 3 articles by Lt.-Col. Jaswant Singh on general aspects of malaria and filariasis. The second and third issues were published in March and May. The Staff of the Bureau of Hygiene and Tropical Diseases welcomes this new publication, and looks forward to papers which, no doubt, will maintain the high standard so long associated with the work of Indian investigators in the mosquito-borne diseases. *Charles Wilcocks*

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